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NEUROPHYSIOLOGICAL AND BEHAVIORAL EFFECTS OF INCIDENTAL IRRADIATION OF NORMAL HUMANS, Final Report for 1 May 1963-August 1969.

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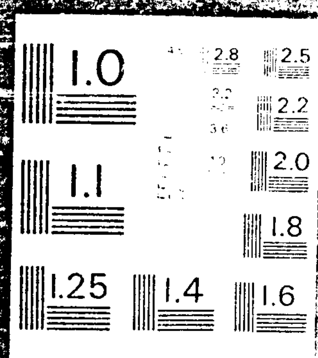

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13. ABSTRACT

The effects of daily Cobalt-60 irradiation on sensory detection of radiation, visual perception, and simple motor performance were investigated in "normal" human subjects during actual and sham irradiation of the apparently normal brain incidental to radiotherapy. The experiments were carried out in both dark and light adapted persons, and it was found that:

a) sensory detection of radiation by humans is not reliable when the phosphene effect is eliminated;

b) visual perception is differentially affected by radiation as a function of the dark-light adaptation state of the retina; and

c) simple motor performance appears to be impaired when central portions of the brain receive about 50 rad. (U)

In addition to these experiments, complex motor performance in multiportal pelvic-irradiated patients was assessed using a modified target gun. The results suggested no reliable posttreatment effects of Cobalt-60 irradiation on complex motor performance under the specified test conditions. (U)

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TABLE OF CONTENTS

ABSTRACT

The effects of daily Cobalt-60 irradiation on sensory detection of radiation, visual perception, and simple motor performance were investigated in "normal" human subjects (Ss) during actual and sham irradiation of the apparently normal brain incidental to radiotherapy. Complete thermoluminescence dosimetry for each S was then performed for specified retinal and intracranial areas (in Rando phantoms). Two experiments were performed to assess Ss' ability to detect radiation, to discriminate flicker fusion, and to perform a simple reaction time task. In Experiment I (Exp. I) the Ss were dark adapted and either head- or neck-irradiated. Head-irradiated Ss were able to detect irradiation 100% of the time, but this was clearly dependent upon the phosphene effect (retinal dose about 50 rads). Detection by neck-irradiated Ss was correct for only 50% of the time and no phosphene effect was evident (retinal dose < 1 rad). The threshold for flicker fusion for head-irradiated Ss was elevated during Cobalt-60 irradiation when compared to pre and postirradiation conditions. Cobalt-60 irradiation had no effect on flicker fusion for the neck-irradiated Ss. Reaction time for head-irradiated Ss in Exp. I did not have the practice effects fully removed from the pretreatment condition. However, when the effects were removed in the neck-irradiated Ss of Exp. I, no effects of irradiation upon reaction time were found.

In Exp. II the Ss were light adapted and head-irradiated. Detection of irradiation for Exp. II Ss was only 50% and no phosphene effect was reported by any light adapted S (retinal dose 36 to 70 rads). The flicker fusion threshold for Exp. II Ss (light adapted) was lower for the irradiation as compared to the sham irradiation condition. In Exp. II, practice effects were removed and reaction time was found to be increased for irradiation as compared to the pre and postirradiation conditions. These findings (Exps. I and II) support the conclusions that: a) sensory detection of radiation by human Ss is not reliable when the phosphene effect is eliminated; b) visual perception is differentially affected by radiation as a function of the dark-light adaptation state of the retina; and c) simple motor performance appears to be impaired when central portions of the brain receive about 50 rad. In addition to Exps. I and II, complex motor performance in multiportal pelvic-irradiated Ss was assessed using a modified target gun. These Ss were tested within 10 min. following daily irradiation and (except in one instance) received only minimal scattered radiation to the brain. Accuracy and error scores for two levels of task difficulty were evaluated. The results suggested no reliable posttreatment effects of Cobalt-60 irradiation on complex motor performance under the specified test conditions.

LIST OF TABLES

LIST OF FIGURES

NEUROPHYSIOLOGICAL AND BEHAVIORAL EFFECTS OF INCIDENTAL IRRADIATION OF "NORMAL" HUMANS

Historically, the nervous system has been considered to be relatively resistant to the effects of ionizing radiation (Furchgott, 1963). During the last two decades, however, significant physiological sensitivity to radiation has been reliably demonstrated. The findings concerning the effects of ionizing radiation have been based primarily upon animal studies utilizing mice, rats, rabbits, dogs, and monkeys (Kimeldorf & Hunt, 1965). To date, relatively little data have been published concerning the neurophysiological and behavioral effects associated with irradiation of the "normal" human brain. The present investigation is an attempt to obtain such data, using patient volunteers undergoing therapy for extracranial neoplasms of the head and neck. Information from this kind of study may be applied to human performance tasks in a radiation environment.

Some areas of the central nervous system (CNS) may unavoidably receive direct or indirect irradiation incidental to the treatment of the head and neck. This has provided us with an opportunity to look at irradiation effects in human subjects (Ss). In order to specify the effect of a given quantity of radiation in human Ss, it was necessary to devise situations in which the degree of change for specific psychophysiological conditions could be measured.

The following areas were selected for investigation: (a) Sensory Detection and Dosimetry [Phase I]; (b) Perception and Performance [Phase II]; and (c) Discrimination [Phase III]. Only the Phase I and II results will be reported here.

Phase I - Sensory Detection and Dosimetry

The sensory responses with the most direct effects on perception and performance were: (a) the phosphene response, and (b) dark adaptation. Head and neck patients may receive significant irradiation of the retina and associated CNS structures. Experiment I (Exp. I) and Experiment II (Exp. II) consider the phosphene effect as a possible visual cue and its relation to dark adaptation for patients undergoing treatment of different body regions. (A medical summary for each patient included in this study is contained in Appendix A.)

Since direct neurophysiological and behavioral effects are apparently related to the amount of radiation reaching certain CNS structures, a systematic dosimetric study of the cranial region was carried out using an Alderson-Rando Phantom. (Details of the phantom dosimetry are given in Appendix B.)

Experiment I

Experiment I was conducted to determine the <u>S</u>'s ability to detect low level irradiation during Cobalt-60 therapy of the

head and/or neck, and to determine if detection is related to dark adaptation. The basic design of both Exps. I and II was to provide periods in which the patient received his radiation treatment, and periods that simulated the treatment (sham trials). Visual and auditory cues were identical during both periods. Verbal reports were taken after each session. The patients of Exps. I and II were treated daily five times a week for six weeks.

Method

Subjects. Experiment I included two Ss treated for carcinoma of the nasopharynx (Ss 1,2); two treated for carcinoma of the larynx (Ss 5,6); and one treated for neck node metastasis (S 3). Table 1 identifies each patient by number, body region exposed, and treatment dosimetry.

Apparatus. A Picker C8M/80 Cobalt-60 teletherapy unit (gamma ray mean energy 1.25 MeV) was used for all radiation treatments. The source to skin distance was 60 or 90 cm. This unit is shown in Figure 16B, page 95.

Control of the radiation beam during Exp. I was obtained with a vertically suspended secondary shutter consisting of a Tungsten block. The block dimensions were 10.5 cm. x 10.5 cm. x 10.0 cm. Figure 1 shows the Tungsten block in the open position, allowing uninterrupted passage of the radiation beam. Figure 2 shows the cover concealing the secondary shutter from S's view.

Table 1

Body Region Exposed, Field Sizes, Total Mean Tumor Exposure, Daily Mean Tumor Exposure, and Exposure Rate at Tumor

Exp.	S	Body Region Exposed	Field Size (cm x cm)	Total Mean Tumor Exposure (R ± 10%)	Daily Mean Tumor Exposure (R)	Exposure Rate at Tumor (R/min.)
I	1	Nasopharyngeal	10x10 bilateral opposing	4900	170	58
	2	Nasopharyngeal	9x11 bilateral opposing	5100	150	52
	3	Neck	11x11 bilateral opposing	5000	150	60
	4	Larynx	Discontinued	-	-	-
	5	Larynx	5x5 bilateral opposing	6300	200	66
	6	Larynx	5x5 bilateral opposing	6500	180	94
II	7	Brain	10x12.5 bilateral opposing	5900	180	42
	8	Retromolar (Nasopharyngeal)	10x12.5 bilateral opposing	6800	200	50
	9	Nasopharyngeal	13x16 bilateral opposing	6300	200	46

(Table continued on following page)

Exp.	S	Body Region Exposed	Field Size (cm x cm)	Total Mean Tumor Exposure (R ± 10%)	Daily Mean Tumor Exposure (R)	Exposure Rate at Tumor (R/min.)
Motor Coordination						(Average for 3 fields)
	10	Pelvic (Bladder) Ant I Post (RPO II) (LPO III)	I. 15x15 II. 10x15 III. 10x15 Coplanar 120° apart	6200	100 50 50 200	60
	11	Pelvic (Bladder) Ant I Post (RPO II) (LPO III)	I. 15x12 II. 10x12 III. 10x12 Coplanar 120° apart	6500	100 50 50 200	42
	12	Pelvic (Bladder) Ant I Post (RPO II) (LPO III)	I. 10x12 II. 10x10 III. 10x10 Coplanar 120° apart	6800	90 45 45 180	46
	13	Pelvic (Bladder) Ant I Post (RPO II) (LPO III)	I. 15x15 II. 10x15 III. 10x15 Coplanar 120° apart	6600	100 50 50 200	52

Note.—All patients were irradiated with Cobalt-60 gamma rays (mean energy, 1.25 MeV). The source to skin distance was either 60 or 90 cm. (For details see Appendices A & B.)

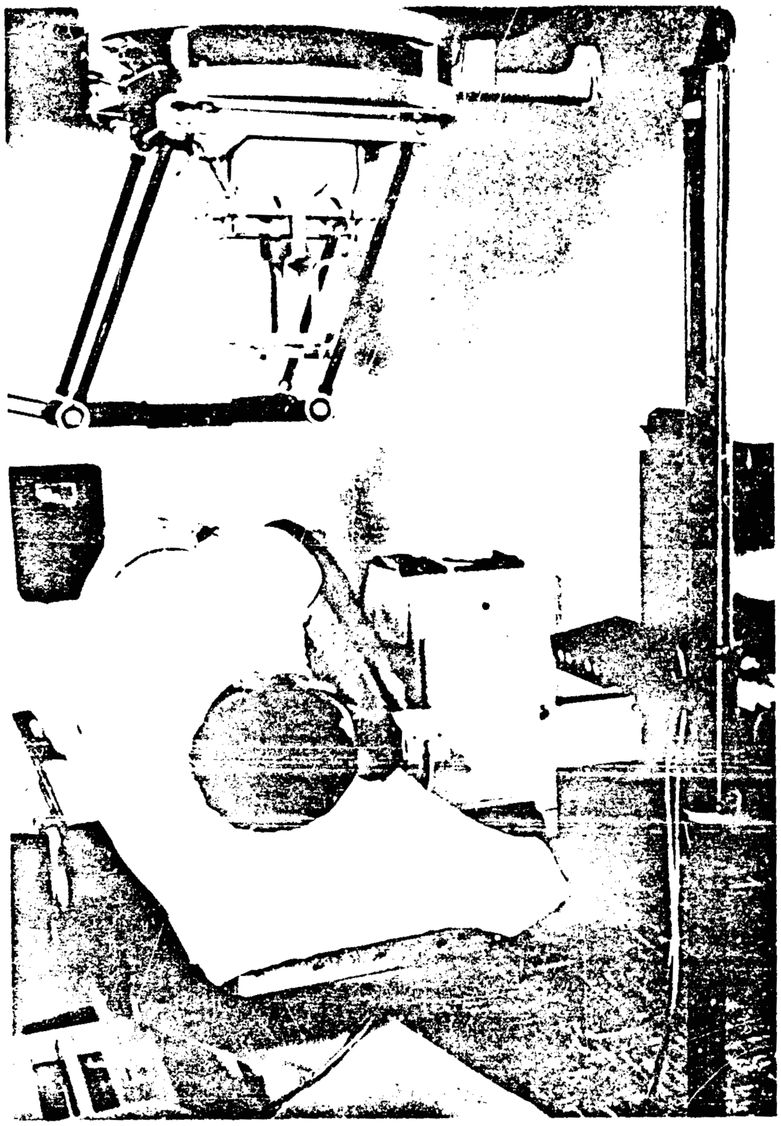

Fig. 1. Patient positioned for treatment in Exp. I. The vertically suspended secondary shutter (Tungsten block) is shown uncovered and positioned out of the beam, i.e., for an actual irradiation period. The stimulus display unit is facing the patient.

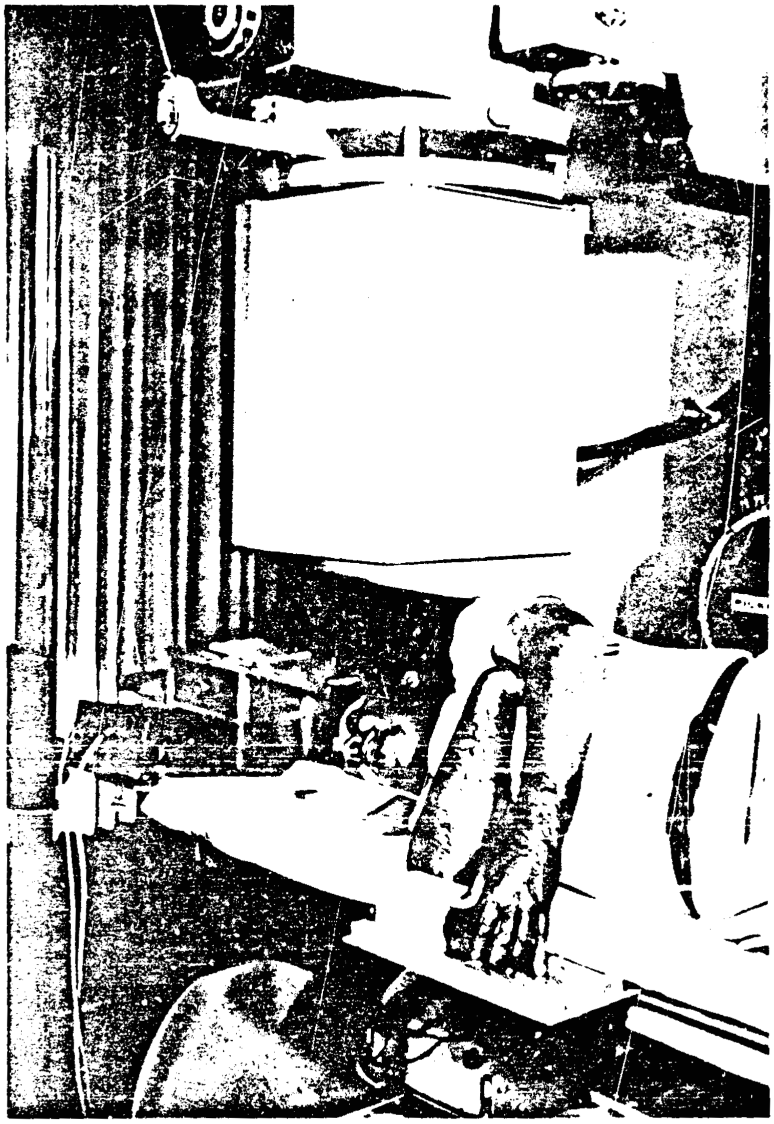

Fig. 2. Patient positioned for treatment in Exp. I. The Tungsten block and its position is concealed from the view of the patient. The stimulus display unit is facing the patient.

The shielded Cobalt-60 treatment room was sound resistant to external noise. The auditory and visual cues associated with the on-off operation of the Cobalt-60 machine were constant for both irradiation and sham trials. With the overhead lights off, the ambient level of illumination in the room was 0.2 log-foot lamberts, which was well within the normal scotopic range of vision.

Procedure. A randomized schedule of actual irradiation and sham irradiation periods during each daily treatment session was used to determine the S's ability to detect irradiation. The sham periods were provided by placing the secondary shutter in the path of the collimated Cobalt-60 beam. The time required for daily irradiation treatment of each S was divided into two equal periods. Two sham periods of equal time were included in each daily session, and all four periods were randomized for each S during each daily session. The randomization sequence was controlled by the therapy technician manually adjusting the shutter, but the specific condition, however, was not known either by the investigator or the S.

Each S (Ss 1,2,3,5,6) was dark adapted for 10 min. prior to testing. In addition, each test period was separated by 3-4 min. during which the technician entered the room, checked the S's position on the table, positioned the secondary shutter, and started the recording system.

Each S was told that some people can tell when they are being irradiated. The operation of the Cobalt-60 machine was

explained and the S was informed that 2 of the 4 periods would be irradiation periods and 2 would be nonirradiation (sham) periods. The S was told that at the completion of each session he would be asked to decide which 2 of the 4 periods were actual irradiation periods. The S was not informed as to the correctness of his decisions.

Results

The Ss treated for nasopharyngeal carcinoma (Ss 1,2) achieved correct detection 100% of the time after the second day of treatment. Upon questioning the Ss, it was determined that their high detection score was associated with a phosphene response. Typical statements by the Ss were, "A curtain of light came out of the machine twice . . . that's when I got the treatment . . ."; or, ". . . a light came on two times but not the other two times . . . I guess I was irradiated when the light came on . . . ." Subjects 1 and 2 correctly associated the phosphene effect with the actual irradiation periods. To verify that the "light" reported by those Ss was due to the phosphene effect, testing was carried on for two successive days without dark adaptation and with the room brightly lighted. Under these conditions, Ss 1 and 2 could not reliably distinguish irradiation from sham periods, i.e., their detection ability reverted to the chance level (50%). It was concluded that Ss 1 and 2 used the phosphene effect to correctly distinguish actual irradiation periods from sham periods when they were dark adapted.

The neck-irradiated patients (Ss 3,5,6) did not reliably distinguish the irradiation from the sham periods, i.e., their choice was at the chance level throughout the course of treatment. They did not report a phosphene effect, nor did they associate any particular sensory experience with their choices. When asked, these Ss frankly stated that they were "just guessing."

Experiment II

Experiment II was designed to determine a patient's ability to detect irradiation without a 10 min. period of dark adaptation, and to note any phosphene response. Apparatus refinements (different from Exp. I) modify procedural aspects of Exp. II.

Method

Subjects. The subjects of Exp. II were two patients treated for nasopharyngeal carcinoma (Ss 8,9) and one (S 7) treated for a brain tumor of rather limited extent. Table 1 (page 4) identifies each patient by number, body region exposed, and treatment dosimetry.

Apparatus. The apparatus was essentially the same as for Exp. I except that Exp. II utilized an improved remotely-controlled shutter as provided for by DASA funds. The new secondary shutter eliminated the 3-4 min. hand-closure delay between the four test periods (Figure 3). The new dimensions of the Tungsten block were 14 cm. x 14 cm. x 18 cm.

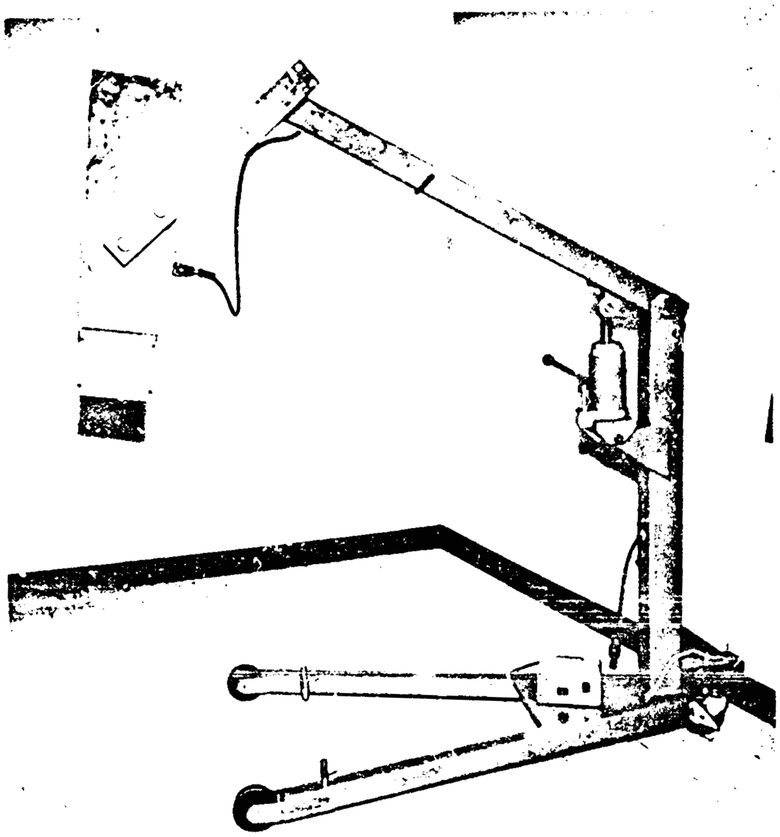

Fig. 3. The remotely-controlled secondary shutter used in Experiment II. The Tungsten block and counterweight are enclosed.

Procedure. In Exp. II, the patients (Ss 7,8,9) were tested under different conditions: (a) no fixed period of dark adaptation; (b) testing procedure was started within less than 3 min. after the room lights were extinguished; and (c) elimination of the time delay. The patients of Exp. II were treated in a supine position with the treatment beam horizontal (Figure 4).

Results

None of the patients in Exp. II could reliably distinguish the irradiation periods from the sham periods. In contrast to the nasopharyngeal carcinoma Ss in Exp. I, the Ss of Exp. II usually said they were "just guessing," as had the neck-irradiated Ss of Exp. I.

To rule out the possibility that the Ss in Exp. II might be experiencing a phosphene effect but were not associating it with 2 of the 4 test periods, the effect was carefully explained to each S during the last ten days of testing, and each S was encouraged to "look" for the occurrence of a "light" when the Cobalt-60 machine was in operation. In spite of the instructions, Ss 7, 8, and 9 did not report "seeing a light," and their detection ability remained at a chance level (50%).

It should be mentioned that no attempt was made in the present study to determine the actual level of dark adaptation. Nevertheless, since Ss 1, 2, 8, and 9 had comparable treatment fields, it would appear that the elimination of the 10 min. period

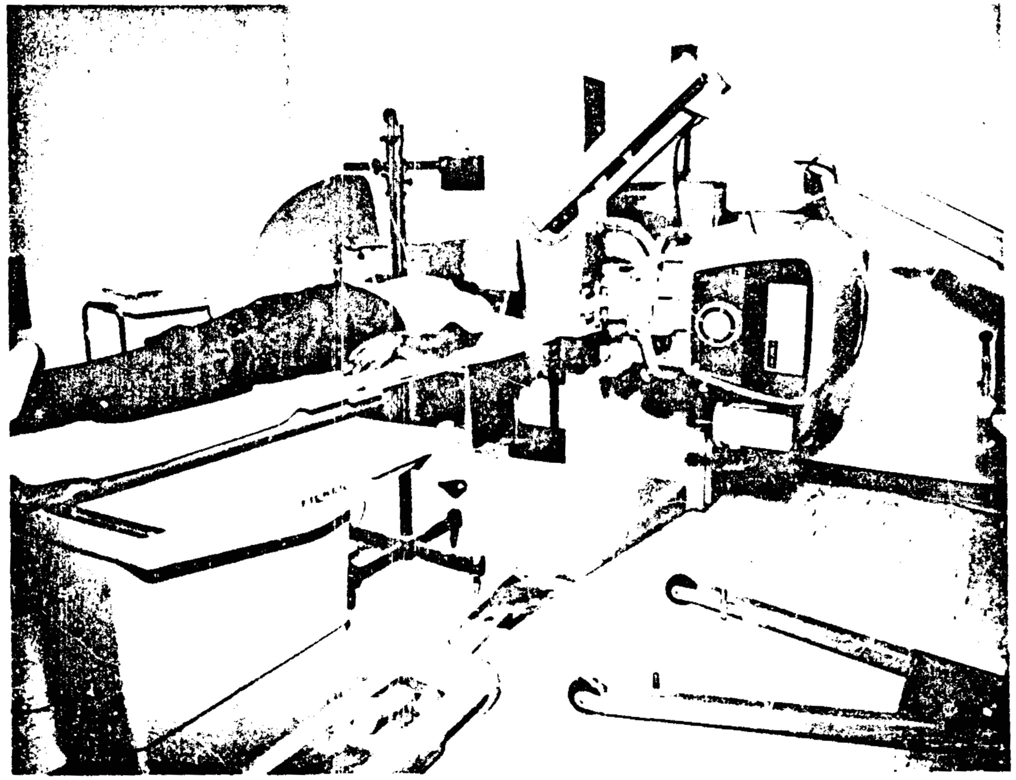

Fig. 4. Patient positioned for treatment in Exp. II. The stimulus display unit is positioned above the patient. The secondary shutter and source head of the teletherapy unit are on the right.

of dark adaptation for Ss 8 and 9 prevented the occurrence of the phosphene effect as a cue for detection of irradiation. Another possible explanation, however, might be the differences in the amount of radiation absorbed by the retina for Ss 1 and 2 as compared to Ss 8 and 9. In order to estimate retinal doses, six dosimeters were placed around the right and left orbits of the phantom as part of the overall head and neck dosimetry study. (The reader is referred to Appendix B for a detailed discussion of the procedure.)

Table 2 shows average retinal dose (rads), average retinal dose rate (rads/min), dark adaptation time (min), detection score (per cent correct), and phosphene response (yes or no). The dose and the dose rate values for the retina are the averages for the lateral, posterior, and medial regions of the right and left retina.

A comparison of the doses, as well as the dose rates, to the retina of the Ss listed in Table 2 indicates that a dose of 49 rads (26 rads/min) induced a clearly defined phosphene effect in S 1 (dark adapted for at least 10 min), while a dose of 70 rads (35 rads/min) did not induce a phosphene response in the essentially light-adapted eye of S 9 (3 min. dark adaptation or less). The differences in dose or dose rate do not appear to be significant, but it seems clear that the dark adaptation state of the retina is critical to the perception of a radiation-induced phosphene effect.

Table 2

Average Dose and Dose Rate for Retina, Dark Adaptation Time, Detection, and Phosphene Response

S/Field	Retinal Dose (Rads)	Retinal Dose Rate (Rads/Min)	Dark Adaptation (Min)	Detection (Per Cent)	Phosphene Response
Nasopharyngeal					
S 1	49	26	10	100	yes
2	55	31	10	100	yes
8	36	17	3	50	no
9	70	35	3	50	no
Neck					
S 3			10	50	no
5	< 1	< 0.1	10	50	no
6	< 1	< 0.1	10	50	no
Brain					
S 7	22	11	3	50	no

Discussion

Sensory detection of low level ionizing radiation was dependent upon the phosphene effect in Ss dark adapted for 10 min. These results suggest that there is a differential sensitivity of rods and cones for radiation. Abis et al. (1955) reported that rod cells are considerably more radiosensitive than cones. Furchgott (1952) reported human studies which suggested that radiation of the skin (2,400 to 6,240 R) increased the scotopic threshold and produced a decrement in dark adaptation level.

In studies of irradiation-induced phosphene response in normal Ss dark adapted (to total darkness for 1 hr.), Gurtovoi and Burdianskaia (1959, 1960) reported a reliable phosphene response with a "dose of only 1 to 3 millirads." However, with a "dose of 0.3 to 0.8 millirads," their Ss did not report a phosphene response. These investigators used an X-ray beam of approximately 33 mm. in diam. with an exposure time of 0.14 sec. to 0.5 sec. (135 kVp, quoted filtration 5 to 8 mm. Cu).

Comparing the results of Gurtovoi and Burdianskaia (1959, 1960) with those obtained in the present study, it appears that, following a 10 min. period of dark adaptation, a retinal dose of about 50 rads will induce a phosphene effect. In contrast, with 1 hr. of dark adaptation, a dose of only 1 mr. has been said to induce the phosphene effect.

The results of the present study indicate that when the phosphene response is masked by light adaptation, detection of radiation is random. Hence, control for dark adaptation is essential for studies of sensory radiation detection. It appears, further, that a more definitive study is needed to evaluate the possible effects of irradiation on the process of dark adaptation per se. This information would help to evaluate man's ability to perform in a darkened environment when subject to irradiation.

Dosimetry of CNS Structures

In addition to the sensory detection study, Phase I included a sufficiently complete dosimetric analysis to determine the dose delivered to all points of interest for each specific field.

The object of this study was to determine the radiation dose absorbed by various peripheral and CNS structures in the cranium in order to aid in evaluating possible effects on sensory and motor systems. Hence, a systematic measurement of dose at points in the head and neck region was carried out for each patient irradiated for extracranial carcinoma.

All measurements were made with thermoluminescent dosimeters (TLD) in an Alderson-Rando Phantom. The treatment geometry for each patient was reproduced and replicate exposures were made. A typical arrangement is shown in Figure 5. The dose was determined for 131 points for each S. The location of these points is shown (Figures 6 and 7) with radiographs of the phantom.

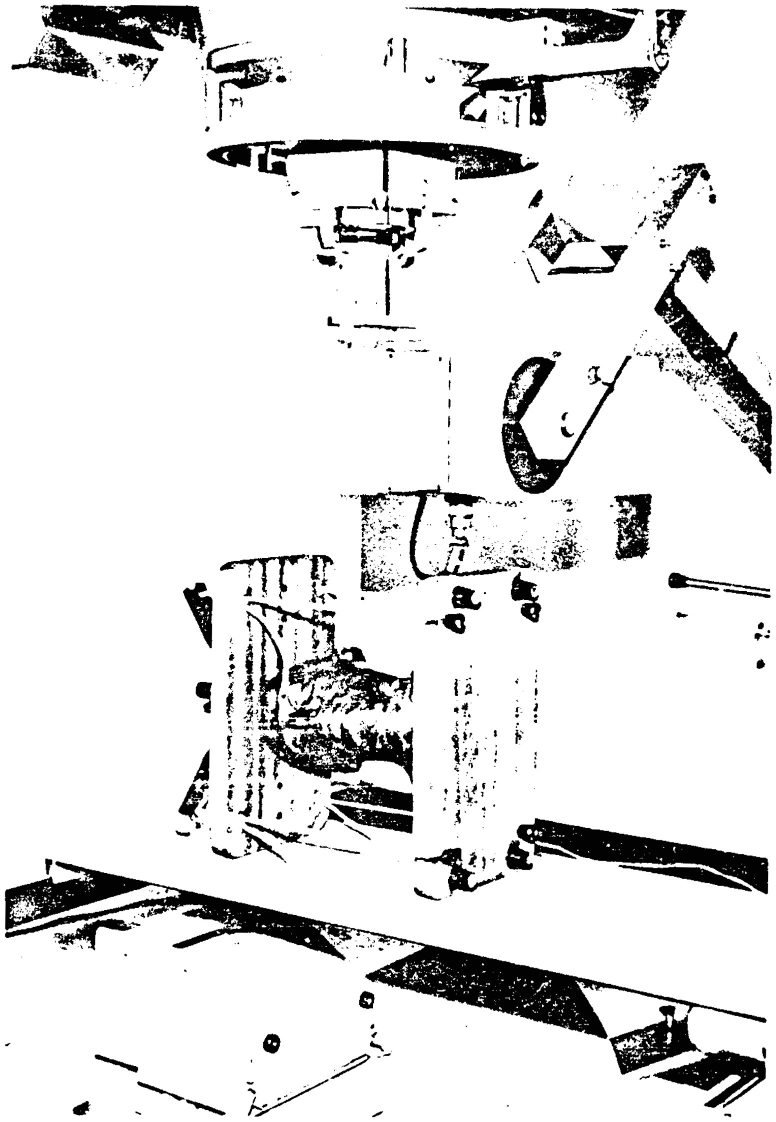

Fig. 5. The Alderson-Rando Phantom positioned for an exposure (Exp. I).

Fig. 6. Radiograph of the phantom (SN 110) (A-P projection). The 131 holes in slabs 1 through 10 have been filled with metal plugs to show the location of the dosimeters.

Fig. 7. Radiograph of the Phantom, lateral projection

The holes which normally receive the tissue-equivalent dosimeters were filled with metal plugs for the radiographs.

The dosimetry results (dose and dose rate) to the retina for Ss in Exp. I and Exp. II of Phase I are shown in Table 2 (page 15).

In Phase II (perception and performance) the dose (rads) to the retina and associated CNS structures was of interest. Table 3 contains the dosimetric results for the retina, optic chiasm, thalamus, motor cortex, and occipital cortex for each S studied in Exp. I and Exp. II.

Complete details of the dosimetry are included in Appendix B.

Table 3

Dose (rad) Absorbed by Retina, Optic Chiasm, Thalamus, Motor and Occipital Cortex (Alderson-Rando Phantom) for One of Two Daily Irradiation Periods

		Peripheral and CNS Area				
Subject	Field	Retina	Optic Chiasm	Thalamus	Motor	Occipital
1	Nasopharyngeal	49	72	42	3	8
2	"	55	75	64	7	15
8	"	36	57	10	2	8
9	"	70	75	46	3	24
3	Neck	< 1	1	< 1	< 1	< 1
5	"	< 1	< 1	< 1	< 1	< 1
6	"	< 1	< 1	< 1	< 1	< 1
7	Brain	22	32	65	75	43

Phase II - Perception and Performance

The purpose of this phase of the investigation was to assess the effects of Cobalt-60 irradiation on perception and performance variables in relation to the amount of radiant energy absorbed by sensory and CNS structures.

Three studies were carried out: (1) visual perception, (2) simple motor performance, and (3) complex motor coordination.

Perception and simple motor performance were investigated in head- and neck-irradiated, dark-adapted Ss in Experiment I (Exp. I) and in head-irradiated, light-adapted Ss in Experiment II (Exp. II). Complex motor performance was studied separately in pelvic-irradiated Ss shortly after daily treatment.

Flicker Fusion and Reaction Time

Flicker Fusion Frequency

An essential function in visual perception is that of resolving power. This is usually thought of as the smallest possible separation of stimuli in space still perceived as separate. The temporal analog of resolving power is flicker fusion frequency (FFF), the smallest possible separation of stimuli in time.

Flicker fusion frequency is that frequency at which the sensation of successive flashes of light become the sensation of a constant or steady light. The experience of a constant or steady light is mediated by the CNS. It is likely that radiation

could affect the threshold and excitability level of the retina, optic nerve, lateral geniculates, or visual cortex.

Reliable measurement of FFF requires precise electronic control of shape, frequency, and light-dark ratio of the pulse driving the stimulus light. In addition, the intensity of the light and area of the stimulus must be constant (Ross, 1938; Winchell & Simonson, 1951; Bartley, 1951; Boswell, 1954).

Other factors that may influence FFF include practice, age, sex, and day-to-day variation related to minor intra-individual biological changes. Misiak (1948) studied practice effects in normal Ss over an 8-week period. He found that after the second session, FFF remained stable and consistent. Similar results were reported by Brozek and Keys (1944). Misiak (1947) studied the effects of age and sex on FFF. He found a significant difference in mean FFF of young Ss (average age 23) as compared to older Ss (average age 74). No significant sex difference appeared for the young or the older group.

The factors discussed above relevant to the reliable measurement of FFF have been controlled in the present study.

Flicker fusion threshold is known to change with the state of dark adaptation. Flicker fusion decreases during dark adaptation. The decrease in FFF for the fovea may be about 3 Hz and slightly more in the periphery for a dark adaptation period (Simonson & Brozek, 1952). Exps. I and II were designed to evaluate possible effects of Cobalt-60 irradiation on FFF for dark- and light-adapted Ss.

<u>Reaction Time</u>

One way of assessing the input-output relations of a stimulus response situation is to look at the speed with which an individual can react to his environment (Underwood, 1966). The classical reaction time (RT) paradigm measures the time interval between the onset of a stimulus and the <u>S</u>s response to that stimulus (Woodworth & Schlosberg, 1954). To the trained <u>S</u>, the stimulus serves to initiate a complex perceptual motor task ending in the response. It is generally thought that a sequence of events must take place before any response is possible; any disruption of the chain is assumed to be reflected by a change in the RT.

The stimulus, or display, sets into operation afferent neuronal activity which, as in this case, involves the visual pathways. Impulses are then projected through the nervous system and the appropriate cortical areas. The path taken by the input determines a course of action which eventuates in various effector mechanisms to produce the designated response. The shortness of RTs across sense modalities gives the individual response a reflex-like character. That other factors are involved, in addition to affector and effector latencies, was shown by Henderson (1952) In a simple RT design involving a visual stimulus and a key pressing task, significant practice effects were observed. Reaction time, then, as a dependent measure, is taken to be a component of larger ongoing processes involving cognitive, motivational, and emotional variables. These latter

variables, however, are thought to contribute minimally in Exps. I and II.

Experiment I

Many investigators, working with animals, have studied the sensitivity of the retina to irradiation (Baylor & Smith, 1958; Avakyan, 1958; Lipetz, 1955). Decrements in b-wave potential and increases in dark adaptation level have been reported (Lipetz, 1955). On the other hand, in a study of the dark-adapted lateral eye of the horseshoe crab (Dawson & Smith, 1959), it was found that the threshold for dark adaptation was reliably lowered by X-ray doses of 5 to 175 rads. The effect could be elicited up to 6 hr. after treatment. The discrepancy between studies is not clear. Studies with human Ss (Motakawa, 1957) suggest that the threshold for the electric phosphene in dark-adapted Ss was increased by as little as 1 rad of X-irradiation. However, it is not known what effect low level ionizing radiation would have on the course and level of dark adaptation for humans.

The object of Exp. I was to study the effects of Cobalt-60 irradiation upon FFF and RT in dark-adapted, head- and neck-irradiated Ss.

Method

Subjects. The Ss were male patients undergoing Cobalt-60 irradiation treatment for extracranial neoplasms of the head (Ss 1,2,8,9) and neck (Ss 3,5,6). The patients were in good physical condition in other respects. Table 1 (page 4) identifies

the S by number, body region irradiated, and treatment dosimetry.

Apparatus. The apparatus for Exp. I consisted of a Cobalt-60 Teletherapy unit, flicker fusion and reaction time equipment, and a Tungsten secondary shutter.

The therapy equipment was a Picker 5000 Rhm Cobalt-60 teletherapy unit, Model C8M/80 (Figure 16B). The flicker fusion apparatus was an Ensco F-111 square wave generator (0.6 to 60 Hz) driving a Sylvania R113B glow modulator lamp. The stimulus light was a circular field 5 mm. in diam. with a constant intensity of .44 millilamberts. The distance from the light field to S's nasion was 27 cm. A spring return response key was depressed by S to indicate when the light appeared "steady."

The reaction time equipment consisted of 4 circular light fields 1.9 cm. in diam. Each light was electrically connected to the response key. Closure of the response key by S turned off the stimulus light. The sequence of light onset to light offset was written on a constant speed chart recorder.

A vertically-suspended, Tungsten secondary shutter (Figure 1, page 6) was used to provide sham irradiation periods.

The treatment room was darkened except for the low intensity zone guard light on the Cobalt-60 unit. The ambient level of illumination was 0.2 log foot lamberts which was in the scotopic range of vision.

Procedure. Initially, each S was dark adapted for 10 min., placed in position for treatment, and carefully trained to

discriminate between a steady and a flickering light. Alternately, S was trained to respond with a key closure to the onset of one of the four RT lights.

Following the initial training, 3 to 5 days of testing and practice were carried out for FFF and RT. Each daily session for each S was divided into four randomized periods (2 irradiation and 2 sham irradiation). Flicker fusion frequency was determined during one actual and one sham irradiation period. Reaction time was measured during the alternate irradiation and sham periods of each daily session.

The threshold for flicker fusion (FFF) was that frequency at which the light first appeared steady (i.e., just 0.5 Hz above the frequency of a light that appeared to flicker). Three to five FFF determinations were obtained during each of the two daily periods.

Reaction time was measured from the chart record of light onset to light offset. Approximately 20 to 30 RTs were obtained during each of the two daily periods.

The multiple FFF and RT measures were obtained for 3 to 5 days preirradiation; for 30 days of Cobalt-60 and sham irradiation; and for 5 days postirradiation. Additional FFF and RT measures were obtained weekly for one month as part of the radiotherapy follow-up procedures.

The Tungsten secondary shutter was manually positioned in or out of the Cobalt-60 beam by the radiotherapy technician. Neither the experimenter nor the S knew the actual position of the secondary shutter during the daily session.

Results

<u>Flicker Fusion Frequency</u> (<u>FFF</u>)

The data for analysis consisted of mean FFF measures for each day of observation. Table 4 contains the mean, standard deviation, number of measures, and standard error for each head-irradiated <u>S</u> in Exp. I. The mean FFF measures in cycles per sec., plotted as a function of irradiation treatment days, are shown in Figure 8 for Exp. I.

Measures for alternate days were used for statistical analysis, thus providing for 2 pretreatment days, 15 treatment days, and 2 posttreatment days. For the purpose of the analysis of variance, FFF data for both Exp. I and II are presented as components of variance in combined form in Table 5.

A paired comparison test was used to evaluate the difference between means for preirradiation, sham, and postirradiation, and first versus second trials. Table 6 contains the results of the paired comparison test for Exp. I. These data indicate that, for Exp. I, there was a significant difference between irradiation FFF mean and pre-post means.

There was no significant difference between the pre and post means, the irradiation and sham means, and the sham and pre-post means. Measure 1 versus 2 is a test for possible order effects since two sets of FFF measures were obtained each day. That this test is not significant, indicates that the order effect was random.

Table 4

Flicker Fusion Means, Standard Deviation (SD), Number of Measures (N),

and Standard Error (S.E.) for Head-Irradiated Patients

Experiment	S	Condition	Mean	SD	N	S.E.
I	1	Pre-	31.2	0.8	8	0.28
		Irrad.	31.7	1.5	36	0.26
		Sham	31.1	1.4	36	0.25
		Post-	31.1	1.8	8	0.67
	2	Pre-	28.1	1.8	8	0.67
		Irrad.	28.7	2.2	36	0.38
		Sham	28.6	2.0	36	0.34
II	8	Pre-	24.8	2.3	8	0.81
		Irrad.	24.5	1.4	36	0.24
		Sham	25.2	1.6	36	0.28
		Post-	25.6	1.2	8	0.44
	9	Pre-	31.9	0.4	8	0.15
		Irrad.	32.3	1.8	35	0.30
		Sham	32.8	1.6	36	0.27
		Post	32.6	1.4	8	0.50

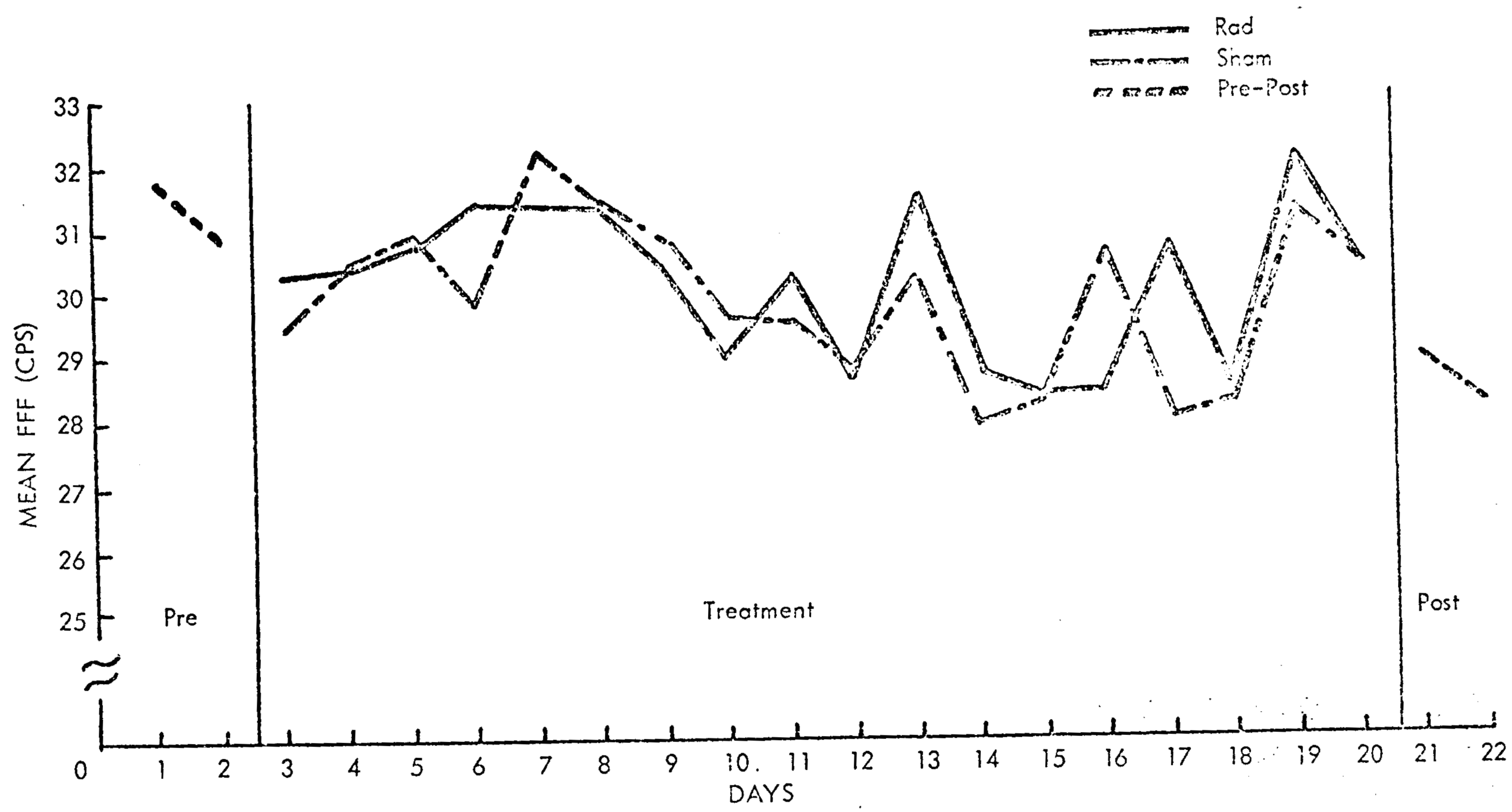

Fig. 8. Mean FFF for Exp. I (dark-adapted, head-irradiated Ss) for pretreatment, treatment, and posttreatment over trial days.

Table 5

Analysis of Variance for Mean FFF for Exps. I and II

Source	*df*	SS	MS	F
Exps. I and II	1	149.43	149.42	
*S*s within experiments	2	2794.58	1397.29	
Days	87	266.77	3.07	1.09
Experiments X days	87	331.40	3.81	
Days X *S*s in experiments	174	489.73	2.81	

Table 6

Paired Comparison Test of Flicker Fusion Means

	Experiment I	Experiment II
Comparison	F	F
Pre vs Post	1.70	1.67
Irradiation vs Sham	3.37	4.86*
Irradiation vs Pre Post	6.11*	1.08
Sham vs Pre Post	0.56	< 1.00
Measure 1 vs 2	2.12	< 1.00

*$p < .05$

Neck-irradiated patients (Ss 3,5,6) were those treated for carcinoma of the larynx and neck. They were dark adapted and followed the same procedure as described for Exp. I. These Ss did not report a phosphene response, and their FFF means were essentially the same throughout the study. Table 7 shows the mean FFF, standard deviation, and number of observations for preirradiation, sham, and postirradiation treatment conditions.

Table 7

Flicker Fusion Frequency Mean, Standard Deviation, and Number of Observations for Neck-Irradiated Ss

Condition	Mean	SD	N
Pre-	27.5	2.8	24
Irradiation	26.6	2.8	72
Sham	27.1	3.2	72
Post-	27.3	1.3	24

A paired comparison test (Table 8) yielded no significant differences between the FFF means. Cobalt-60 irradiation of 60 to 94 rad/min. to a somewhat small field of the neck (5 cm x 5 cm) did not modify visual perception. These results are likely due to the fact that less than 1 rad of scattered irradiation reached the retina and associated CNS structures

Table 8

Flicker Fusion Frequency Paired Comparison Test

for Neck-Irradiated Ss

Comparison	F	p
Irradiation vs Sham	1.20	$< .10$
Irradiation vs Pre-Post	3.68	$< .10$
Sham vs Pre-Post	3.22	$< .10$

for the neck-irradiated Ss as compared to the head-irradiated Ss who received 30 to 90 rads to the retina and CNS structures (Table 3, page 22).

Reaction Time

Each daily block of 25 to 30 RT trials was averaged. The interstimulus interval (ISI) was approximately 1 sec. The distribution of RT measures as a function of days is shown in Figure 9. Table 9 contains the mean, standard deviation, number of measures, and standard error for each condition of Exp. I. For purposes of analysis, the daily mean RT measures were evaluated using an analysis of variance with Exps. I and II included as components of variance. The results of the analysis of variance are shown in Table 10.

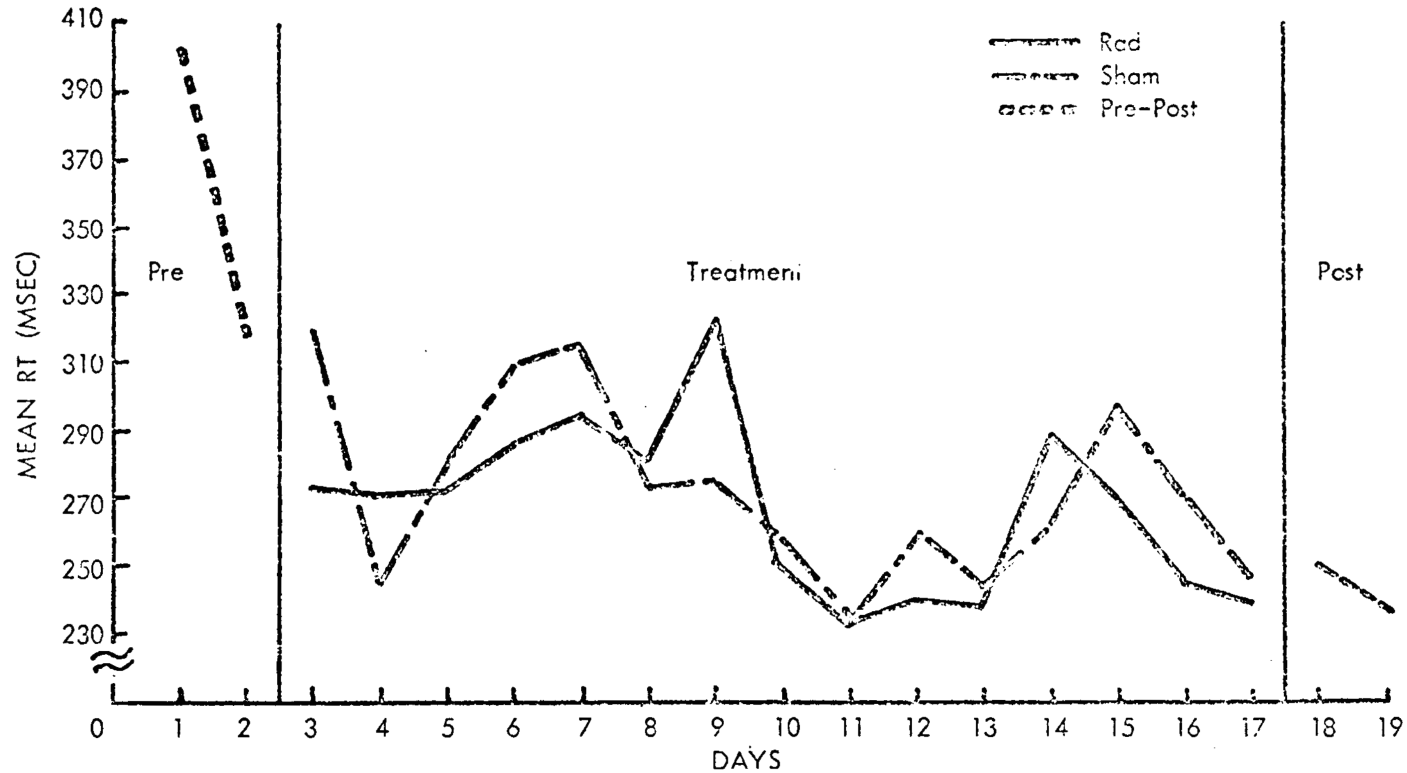

Fig. 9. Mean RT for Exp. I (dark-adapted, head-irradiated Ss) for pre-treatment, treatment, and posttreatment over trial days.

Table 9

Reaction Time (RT) Mean for Each Condition, Standard Deviation (SD), Number of Observations (N), and Standard Error (S.E.) for Experiment I and Experiment II

Experiment	S	Condition	Mean	SD	N	S.E.
I	1	Pre-	327.3	58.9	8	20.8
		Rad	233.2	55.7	30	10.1
		Sham	239.1	48.1	30	8.8
		Post-	198.4	38.0	8	13.5
	2	Pre-	381.1	103.4	8	36.6
		Rad	302.5	20.7	30	3.8
		Sham	308.7	27.9	30	5.1
		Post-	287.1	16.9	8	6.0
II	8	Pre-	291.3	18.5	8	6.5
		Rad	322.4	32.3	30	5.9
		Sham	315.1	24.9	30	4.5
		Post-	314.7	18.7	8	6.6
	9	Pre-	227.4	15.9	8	5.6
		Rad	239.2	17.8	30	3.2
		Sham	239.1	23.5	30	4.3
		Post-	225.7	8.4	8	3.0

Table 10

Analysis of Variance of Mean Reaction Time for Exps. I and II

Source	df	SS	MS	F
Exps. I and II	1	37.39	37.39	
Ss within experiments	2	422030.26		
Days	75	130798.33	1743.98	1.33
Experiments X days	75	187191.19	2495.88	
Days X Ss within experiments	150	196288.72	1308.59	
Total	303			

A paired comparison test was used to evaluate the difference between pairs of means as shown in Table 11.

Although the comparison of means for pre versus post, irradiation versus pre-post, and sham versus pre-post were significant, it appears that the practice effect for RT was not fully removed from the pre measures; hence these results are not reliable. However, the preirradiation practice effects were fully removed for Exp. II.

The neck-irradiated Ss (S 3,5,6) followed the same procedure. Analysis of variance and paired comparison tests yielded no significant changes in RT. The retina and CNS structures of these Ss received less than 1 rad/min.

Table 11

Paired Comparison Tests for Reaction Time Means

Comparisons	Experiment I F	Experiment II F
Pre vs Post	20.07**	1.48
Irradiation vs Sham	< 1.00	< 1.00
Irradiation vs Pre-Post	9.85**	8.50**
Sham vs Pre-Post	6.35*	5.01*
Measure 1 vs 2	< 1.00	1.82

*$p < .05$

**$p < .01$

Experiment II

Experiment II followed essentially the same method as described for Exp. I except that the Ss were light adapted. Some of the results for Exp. II have been presented in the Results Section for Exp. I due to the nature of, and assumptions of, the analysis of variance. Experiment II will be reported summarily to maintain continuity of the report.

Subjects. Exp. II Ss (Ss 7 8,9) were head-irradiated. Subject 7 was irradiated for a brain lesion and was not included in the analysis of the data for Exp. II.

Apparatus. The apparatus was the same as that described for Exp. I with two exceptions: (1) a remotely-controlled secondary shutter (purchased with DASA funds) was used to provide sham irradiation periods; and (2) an event timer was used to record RT. This timer measured the time between onset and offset of the stimulus light in 1/100 sec. intervals.

Procedure. The Ss in Exp. II were light adapted as compared to the dark-adapted Ss of Exp. I. The measurement procedure for FFF and RT was the same as Exp. I with the exception that RT was read from the timer and recorded by the investigator after each stimulus response trial.

Results

Flicker Fusion Frequency

The distribution of the daily mean FFF in cycles per sec. for preirradiation, sham and postirradiation are shown in Figure 10. Table 4 (page 30) contains the FFF means, standard deviation, number of observations, and standard error for Exp. II.

For Exp. II the FFF mean for sham was significantly higher than the irradiation mean; all other mean FFF comparisons (Table 6, page 32) were insignificant.

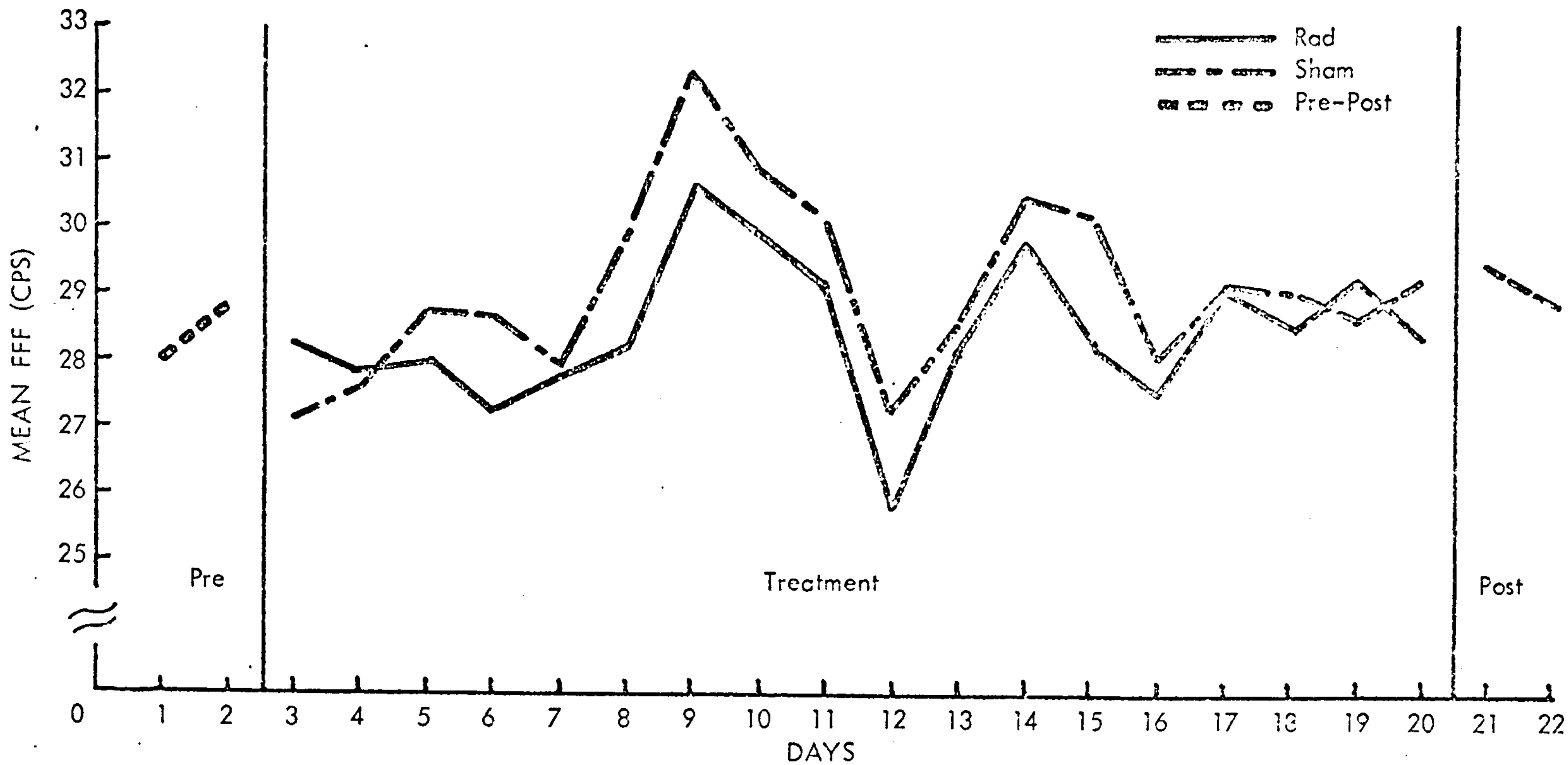

Fig. 10. Mean FFF for Exp. II (light-adapted, head-irradiated Ss) for pre-treatment, treatment, and posttreatment over trial days.

The combined mean FFF for Exp. I and Exp. II as a function of pretreatment and posttreatment conditions is shown in Figure 11.

The FFF data were further analyzed to test for possible carryover effects. A 24-hr. carryover effect was tested using the daily FFF measure taken at least 24 hr. following irradiation. A 72-hr. carryover effect was tested using the data for Friday and Monday. Both irradiation versus sham and sham versus sham means were compared for the 24- and 72-hr. periods. No significant differences were found for carryover periods of 24 and 72 hr.

Reaction Time

The distribution of RT measures as a function of days is shown in Figure 12 for Exp. II. Table 9 (page 36) contains the mean, standard deviation, number of measures, and standard error for each condition in Exp. II. The daily mean RT measures were evaluated using an analysis of variance with Exps. I and II included as components of variance. The results of the analysis of variance is shown in Table 10 (page 37).

Paired comparison tests for Exp. II are shown in Table 11 (page 38). Practice effects were fully removed from these data for Exp. II. Hence, the comparison between means indicates a reliable effect of irradiation. The mean RT for irradiation and for sham were significantly increased as compared to pre and post RT means. All other comparisons were not significant.

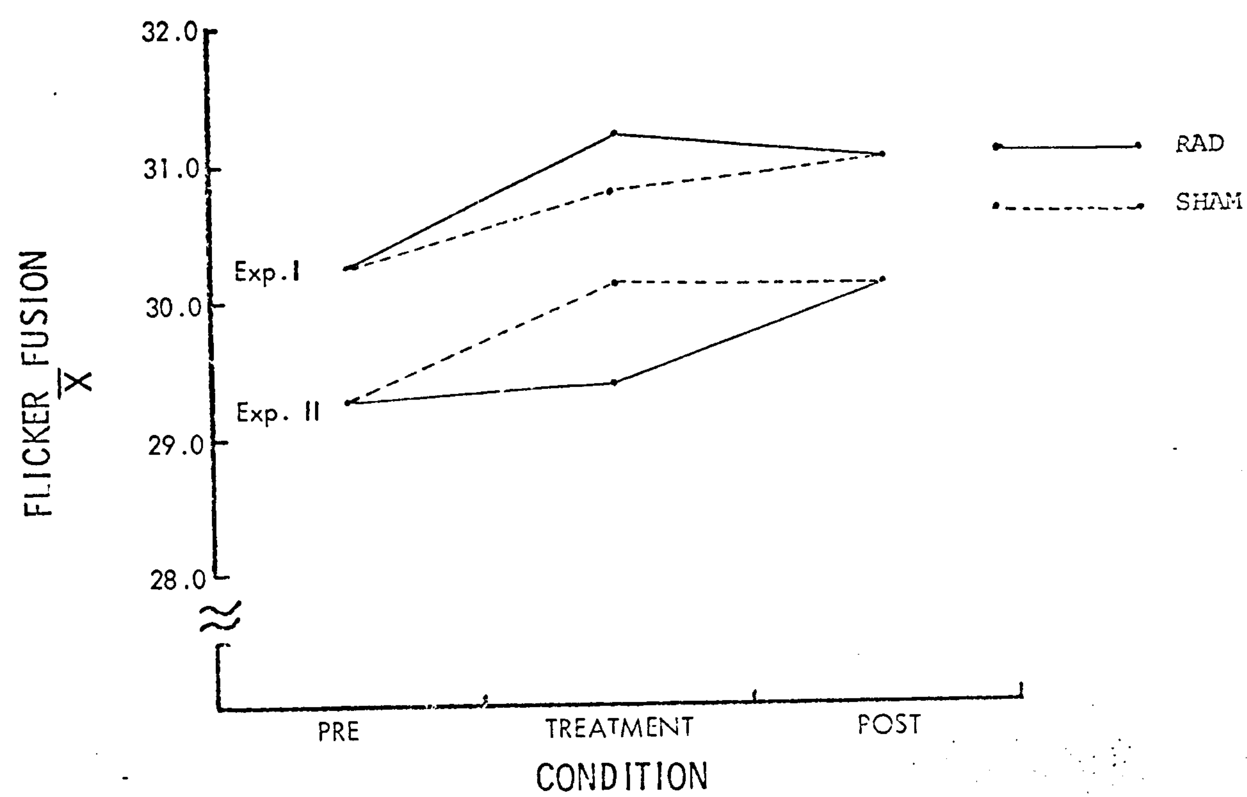

Fig. 11. Combined mean FFF for Exp. I and Exp. II (head-irradiated Ss) for pretreatment, treatment, and posttreatment conditions.

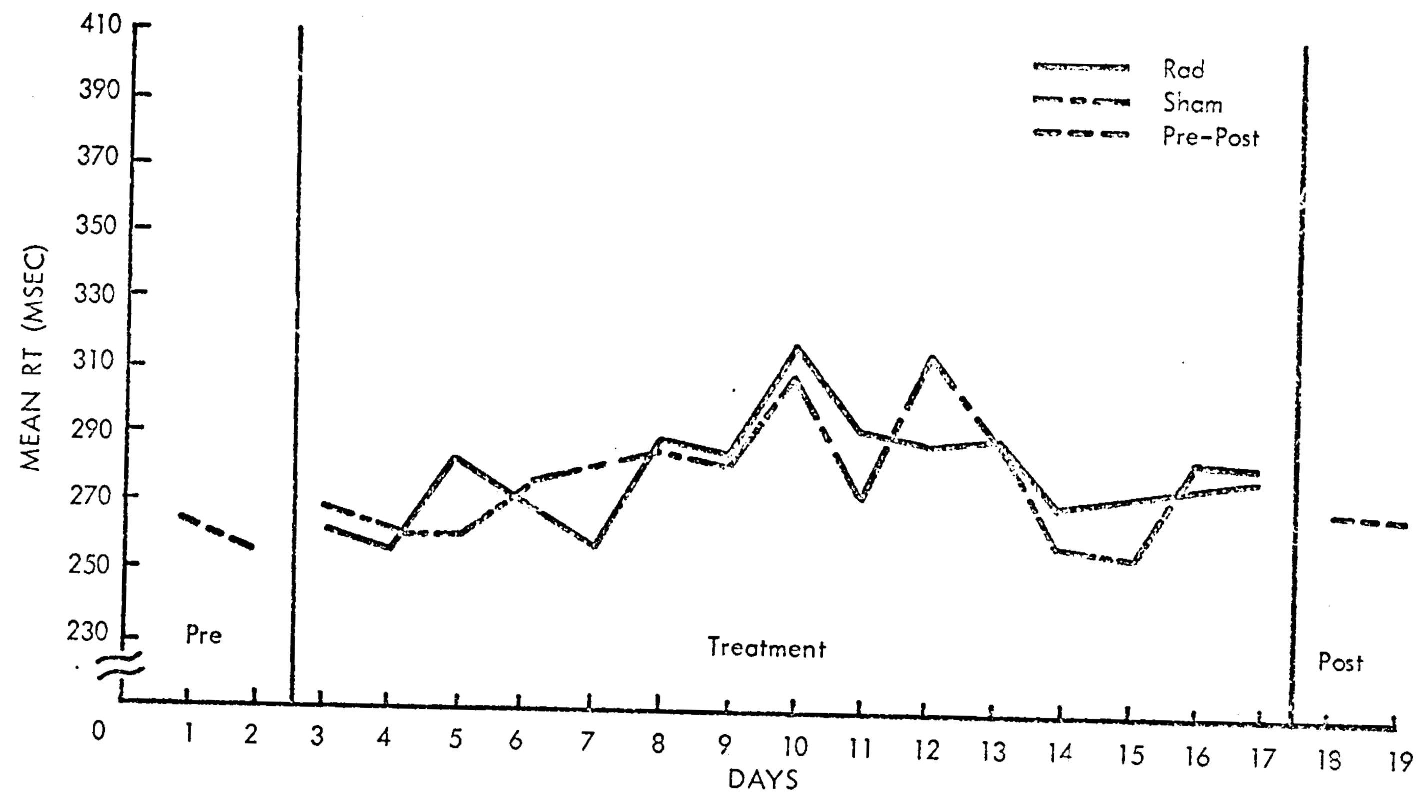

Fig. 12. Mean RT for Exp. II (light-adapted, head-irradiated Ss) for pretreatment, treatment, and posttreatment over trial days.

The combined RT means for Exp. I and Exp. II as a function of pretreatment, irradiation sham, and posttreatment are shown in Figure 13. It should be noted that the mean for Exp. I pretreatment condition is elevated since the practice effect had not been removed. However, the distribution for Exp. II (Figure 13) is free from practice effects and represents a real effect of irradiation.

Discussion

Flicker Fusion

Flicker fusion frequency (FFF) as a measure of perceptual discrimination requires a stimulus that is constant in brightness, area, and distance from the cornea. Under these conditions the fusion threshold may vary due to retinal and/or CNS changes in excitability incidental to low level ionizing irradiation. Since the retina is one receptor that responds to radiation, some perceptual abnormality or distortion could be expected due to retinal receptor changes. However, CNS structures may be modified in addition to the receptor (retinal) changes.

The results of Exp. I indicate that the flicker fusion threshold for the dark-adapted retina is elevated during irradiation as compared to the pre- and post-control conditions. The dark-adapted retina allows the use of the more sensitive rods to mediate vision; hence, the FFF should be higher than for the light-adapted retina mediated by the less sensitive cones.

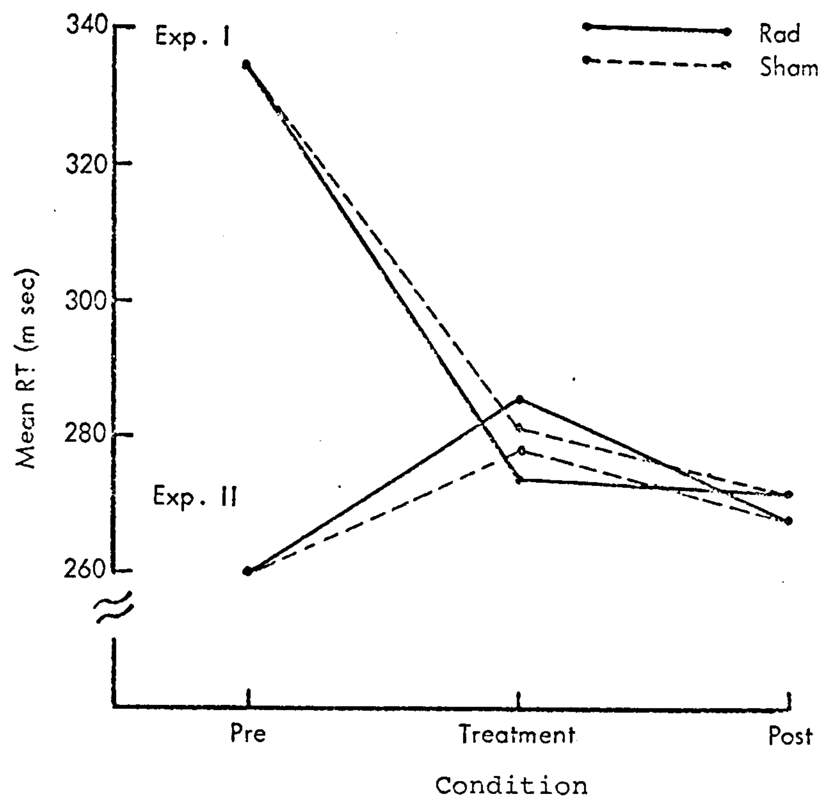

Fig. 13. Combined mean RT for Exp. I and Exp. II (head-irradiated Ss) for pretreatment, treatment, and posttreatment conditions.

A dose rate (Table 3, page 22) of 40 to 54 rad/min. to the retina and 70 to 75 rad/min. to associated CNS structures will raise the FFF threshold in the dark-adapted retina. This finding is supported, in part, by studies of the threshold for the electrical phosphene response in dark-adapted human Ss (Motakawa, 1957). The threshold for the electrical phosphene was elevated by as little as 1 mr. of X-irradiation.

The results for Exp. II Ss (light-adapted, essentially cone vision) showed a significantly lower FFF threshold for the irradiation trials as compared to the sham trials. The dose rate to the retina (Exp. II Ss) was 36 to 70 rad/min. and 57 to 75 rad/min. to associated CNS structures. Since the dose rate was comparable for both Exp. I and II Ss, it is likely that the differential responses in FFF is a function of the different retinal receptors (i.e., rods vs cones) associated with the adaptation state of the retina. Thus, perceptual discrimination in the dark-adapted state may be facilitated (Exp. I), but in the light-adapted state, perceptual discrimination may be impaired by low level ionizing radiation (Exp. II). These results are for brief exposures of 1.5 min. to 3 min. and relatively low dose rates. Increased dose rates and/or longer exposures might be expected to increase the perceptual decrement for the light-adapted retina.

Since no significant carryover effects were observed for either Exp. I or Exp. II, it is likely that the effects of low level ionizing radiation on perception are transient, lasting, at most, for several minutes for the light-adapted retina.

However, the effects on the dark-adapted retina may persist for longer periods since no significant difference between irradiation and sham FFF was found. Studies on radiation-induced threshold changes for the electrical phosphene (Motakawa, 1957) indicated that the increase in threshold for the dark-adapted retina persisted for several days.

<u>Reaction Time</u> (<u>RT</u>)

There was a significant difference between the pre- and post-RT means for Exp. I, but not for Exp. II (see Table 11, page 38). This difference for Exp. I was probably due to continued practice effects. The Exp. I <u>S</u>s were given 3 days practice and 2 days pretreatment. However, the Exp. II <u>S</u>s were given 5 days practice and 2 days pretreatment. There was no significant difference between irradiation and sham RT means for either Exp. I or Exp. II.

The neck-irradiated patients did not show significant differences in RT when CNS structures in these patients received less than 1 rad. No significant difference in RT was noted among the head-irradiated, dark-adapted <u>S</u>s of Exp. I as compared to the light-adapted <u>S</u>s of Exp. II. If the practice effect is fully removed, the expected RT curve is that shown in Figure 13 (page 45) for Exp. II <u>S</u>s.

It thus appears that RT, as a measure of motor response, is not differentially modified during Cobalt-60 irradiation as compared to sham measures obtained within 3 to 5 min. for

Exp. I and about 2-3 min. for Exp. II. There is a significant difference in RT for irradiation and sham means as compared to pre-post means for both Exp. I and for Exp. II. However, these differences for Exp. I are again confounded with the practice effects. The increase in irradiation and sham means during the treatment condition for Exp. II is reliable since practice effects were fully removed. Figure 13 (page 45) shows the means for pre-irradiation, irradiation, sham irradiation, and postirradiation conditions for Exp. I and Exp. II. These results suggest that Cobalt-60 doses to the human CNS of 36 to 70 rads will increase RT as compared to pretreatment and posttreatment control periods.

The lack of a significant separation between the irradiation RT and sham RT may reflect an extended effect of irradiation persisting for several minutes. It is difficult to separate the initial stimulus effect on the CNS and the additional perceptual consequences that could be present. Since RT involves successive processing (Smith, 1967), i.e., sensory input, followed by response selection, followed by response performance, it is most likely that the response selection stage mediated by the CNS is modified by low level ionizing radiation. The evidence from irradiation conditioning studies (Kimeldorf & Hunt, 1965) has suggested mutually facilitated or coordinated effects of radiation stimulation and motivation. However, other evidence indicates that these effects can act disjunctively (Kimeldorf & Hunt, 1965, p. 207), producing a response pattern of confusion. Acting as a distributed stimulus on neuronal processes, radiation could generate

perceptual distortions, i.e., changes in threshold (as shown in the previous section on perception). Alternatively, irradiation could interfere with the response selection stage of motor performance. In this case, the human operator may experience momentary "confusion" (delay) in carrying out motor responses. This is likely to occur when motivation is at a low level, e.g., when performing a simple task that has low cognitive and emotional requirements.

Complex Motor Coordination Task

Previous studies discussed in Phase I and Phase II were carried out with patients receiving irradiation directed either to the nasopharyngeal region (head) or larynx (neck). These studies used irradiation-sham sequences during daily treatment sessions. However, possible effects of irradiation on complex motor performance immediately following daily treatment sessions had not yet been investigated. A modified electronic target apparatus was therefore used to evaluate daily postirradiation effects on complex motor coordination.

The patient, in a standing position, was required to align precisely a target gun and shoot as rapidly and accurately as possible at stationary or moving targets. This task was carried out within 5-10 min. following multiportal irradiation of a relatively generous body volume (pelvis). Data were also presented for one patient (S 7) who was irradiated for a brain tumor of rather limited extent (Oligodendroglioma of the left Rolandic fissure adjacent to the midline).

Method

Subjects. The Ss were five adult males, Ss 7,10,11,12,13 (Table 1, page 4) undergoing Cobalt-60 irradiation treatment in the Radiotherapy Section of the Veterans Administration Hospital. Criteria for selection was ability to meet physical requirements and willingness to participate in the study. All patients were

alert, ambulatory, and felt reasonably well. Five employees of the Radiotherapy Section were used as control Ss to obtain normative data concerning the practice effect.

Apparatus. The testing equipment was a standard electronic target apparatus with two rows of stationary targets, pop-up targets (2 in front, 1 in rear, 3 in doorways), and 3 moving figures on the back panel of the apparatus. Each shooting task was limited to 60 sec. A cumulative score was calculated automatically and prominently displayed at the front window. Two electrical counters were attached to the machine to record the number of shots fired and the number of targets hit during each shooting task. The error score obtained from these counters was subsequently analyzed.

Procedure. The purpose of the experiment was fully explained and each S was given time to become familiar with the apparatus. Subjects were allowed 2 familiarization trials each for an easy (A) and difficult (B) task. After the initial familiarization, S was told to report back the next day to begin the practice period.

The shooting task in this study required two levels of difficulty in eye-hand coordination skill (A & B). Since motor skill improves with practice, control Ss shot for 5 days, and daily scores were evaluated to determine the number of days required to reach a stable adjusted error score. This point was reached in 3-4 days; hence, the first 4 days of practice constituted the practice period.

During the A (easy) task, S was allowed to shoot at any of the stationary or pop-up targets. During the B (difficult) task, S could shoot only at the moving figures. A random schedule of shooting order was established for the A and B tasks.

The fifth day was considered as a pretreatment measure for statistical analysis. Subjects began irradiation treatment on the sixth day and performed 2 A and 2 B tasks immediately after each daily treatment.

On the first practice day the S was read the following instructions:

> We are studying the possible effects of small dose irradiation treatments upon human performance. Target shooting is one method of measuring human performance. It is important that you do your best and try to get as high a score as possible. Coupon books, which may be used at the Canteen, are given for Bonus Scores on either an A task or B task. The target gun has two rows of stationary targets, two pop-up targets in front, and a pop-up target in the rear. It also has three moving figures on the back panel of the machine. Before each game you will be told if it is an A or B task. When you are instructed to shoot an A task, you may shoot at any of the targets EXCEPT the three moving figures. You may shoot the targets in any order you wish. When you are instructed to shoot a B task you are to shoot at ONLY the three moving figures. You may shoot in any order you wish. Both the A and the B task have a time limit of 60 sec. in which you may fire as many shots as you wish. Do not discuss your score with other participants in the study. Are there any questions?

During each task, S fired as many shots as possible during a 60-sec. period. His motivation for achieving a high score was enhanced by paying him a bonus ($1 canteen coupons) when he exceeded his previous average accuracy score. After each task the investigator recorded the number of hits and total number of shots fired on the data sheet (Appendix C). The adjusted

error (Ae) was calculated by comparing the ratio of the actual number of hits to the number of shots fired against the number of hits and shots possible during each task. (The electrical mechanism allowed a maximum of 36 shots per 60 sec.)

The following formula was used to calculate the Ae score:

$$X = \frac{36y}{z} \qquad 36 - X = \text{Ae score}$$

(y = number of hits and z = number of shots fired.)

Results

Data were arranged into blocks of days. Each block represents the mean of several days (Figure 14). Block 1 represents the practice period (4 days). Block 2 represents the pretreatment period (last day before treatment began). Blocks 3-7 represent the treatment period. Each block during the treatment period represents the mean of an equal number of days. Block 8 represents the posttreatment period (5 days).

Accuracy and Rate. The mean number of hits and shots for the A and B tasks was calculated and a 1-way analysis of variance was computed for each set of data.

The data were analyzed for possible changes in rate of firing (shots) and accuracy of firing (hits). The distribution of the mean A shots and mean A hits, shown in Figure 14, is not reliably related to irradiation as administered in this study. The F ratios for A shots (Table 12) which was $F_{4,35} = 0.51$, $p > .10$ and for A hits (Table 13) which was $F_{4,35} = 0.57$, $p > .10$ are not statistically significant.

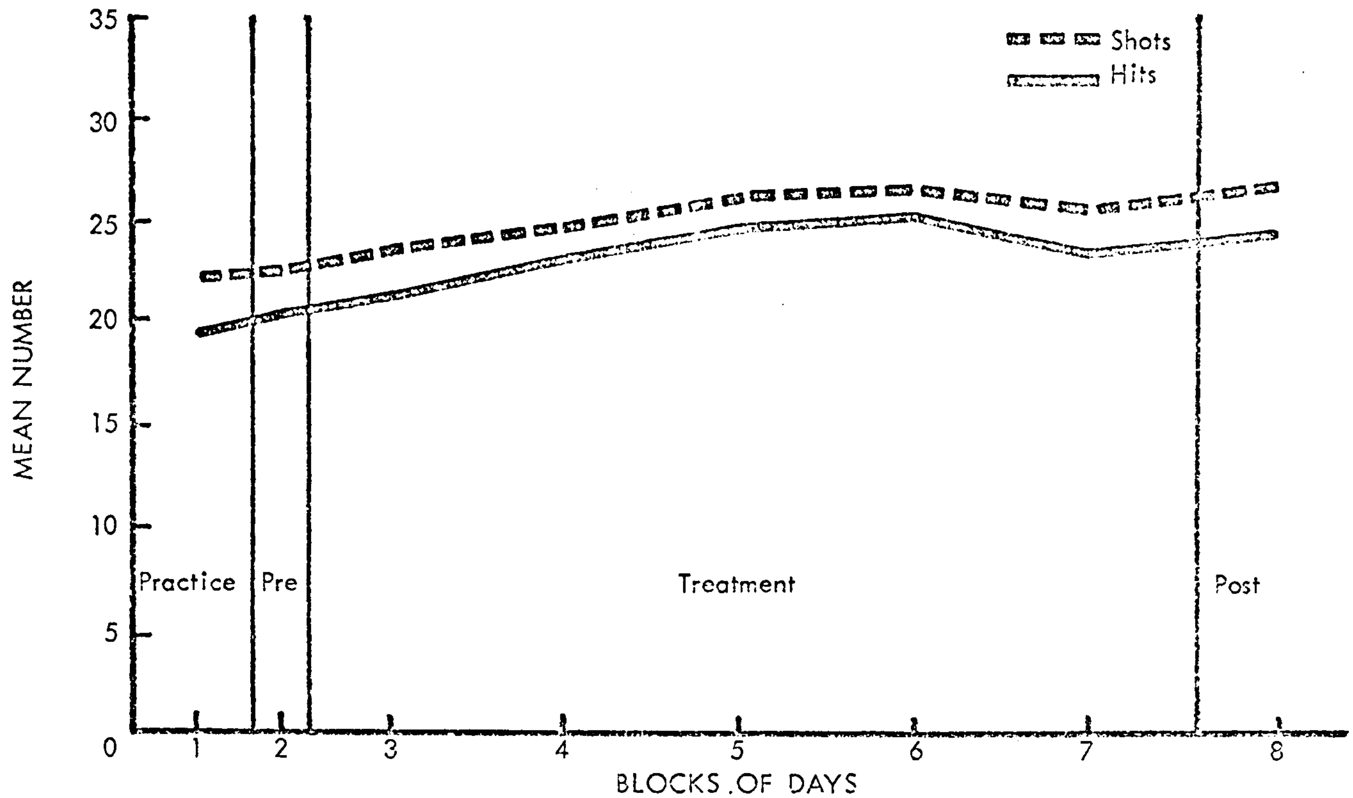

Fig. 14. Mean number of shots and hits for Task A during practice, pretreatment, treatment, and posttreatment periods. Blocks of days represent data averaged for five consecutive days.

Table 12

Analysis of Variance of Mean Number of Shots for Task A

Source of Variance	SS	df	MS	F
Between Blocks of Days	112.31	4	16.04	0.51
Within Ss	1000.98	35	31.28	
Total	1113.29	39		

Table 13

Analysis of Variance of Mean Number of Hits for Task A

Source of Variance	SS	df	MS	F
Between Blocks of Days	144.19	4	20.60	0.57
Within Ss	1166.56	35	36.46	
Total	1310 75	39		

Similar results were obtained for the difficult (B) task. The distribution of the means for task B, shown in Figure 15, was not reliably affected by irradiation.

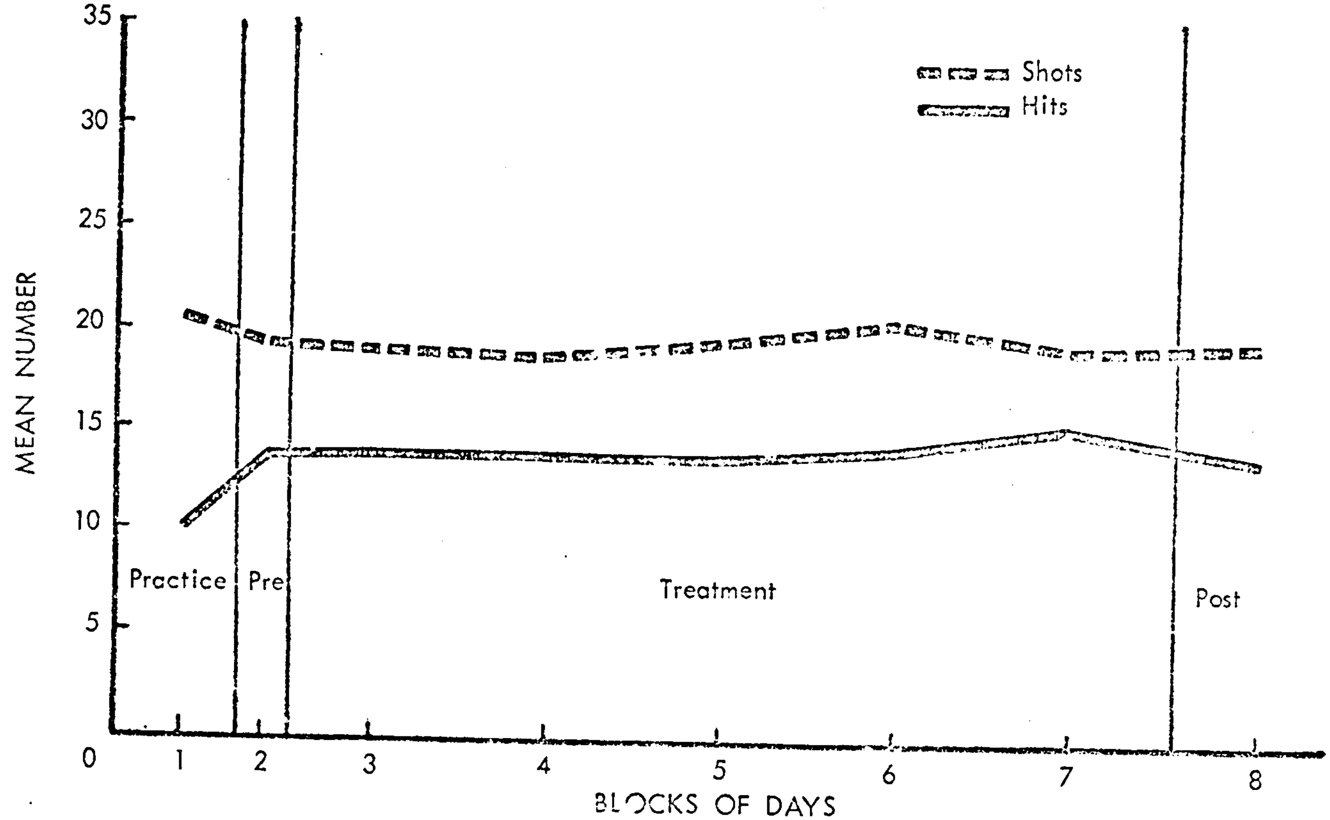

Fig. 15. Mean number of shots and hits for Task B during practice, pretreatment, treatment, and posttreatment periods. Blocks of days represent data averaged for five consecutive days.

The analysis of variance for B shots (Table 14) and B hits (Table 15) yielded F ratios of $F_{4,35} = 0.06$, $p > .10$ for shots, and $F_{4,35} = 0.26$, $p > .10$ for hits, which also were not statistically significant.

Table 14

Analysis of Variance of Number of Shots for Task B

Source of Variance	SS	*df*	MS	F
Between Blocks of Days	10.75	4	1.54	0.06
Within Ss	858.13	35	26.82	
Total	868.88	39		

Table 15

Analysis of Variance of Mean Number of Hits for Task B

Source of Variance	SS	*df*	MS	F
Between Blocks of Days	77.60	4	11.09	0.26
Within Ss	1372.42	35	42.89	
Total	1450.02	39		

The mean number of shots and hits for the A and B tasks for S 7 are shown in Figures 16 and 17, respectively. These data are shown separately for purposes of comparison since the patient was treated for brain tumor (presumably localized to the Rolandic fissure region). The S received an average dose rate at the tumor of 41.7 rad/min. An inspection of Figures 16 and 17 indicates that S's performance was very stable and was similar to the performance of the other patients.

Performance Error. The adjusted error scores (Ae, see page 53) for the A and B task are a measure of the rate, or magnitude, of performance error. The Ae measured were transformed to log (X + 2) to obtain a log normal distribution for statistical analysis. Figure 18 shows the mean log error for the A and B tasks as a function of blocks of days. A factorial analysis of variance, using 5 (Ss) X 2 (1st and 2nd trials) X 8 (blocks of days), was computed to evaluate the rate and magnitude of error. The results of this analysis are shown in Table 16.

The F ratios for Ss, trials, and days were not significant ($p > .10$); hence no reliable difference in rate and magnitude of performance error was associated with irradiation as compared to pre and posttreatment performance for the difficult (B) task. The analysis of the results for the above complex motor performance tasks A (easy) and B (difficult) indicates that there was no reliable change in rate of firing,

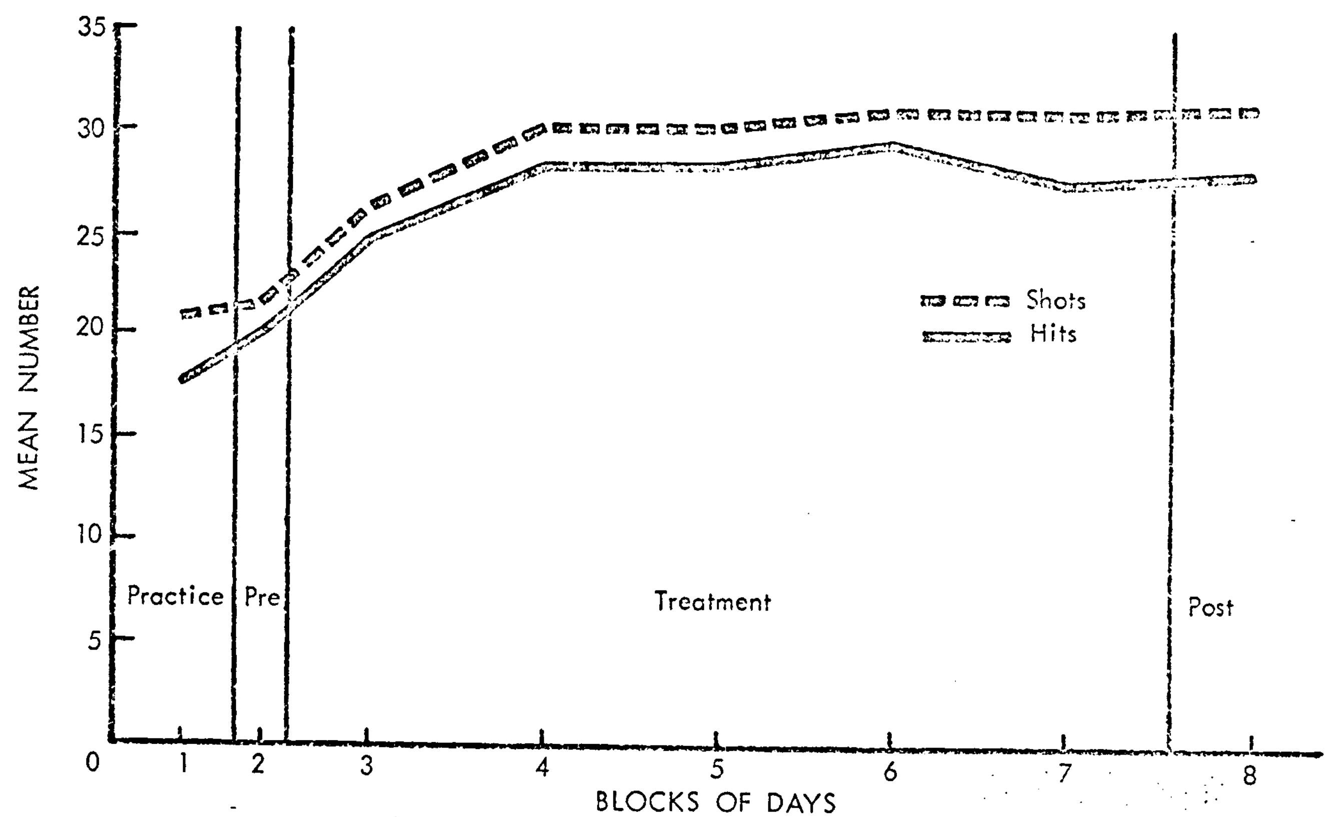

Fig. 16. Mean number of shots and hits for Task A for S 7 only during practice, pretreatment, treatment, and posttreatment periods. Blocks of days represent data averaged for five consecutive days.

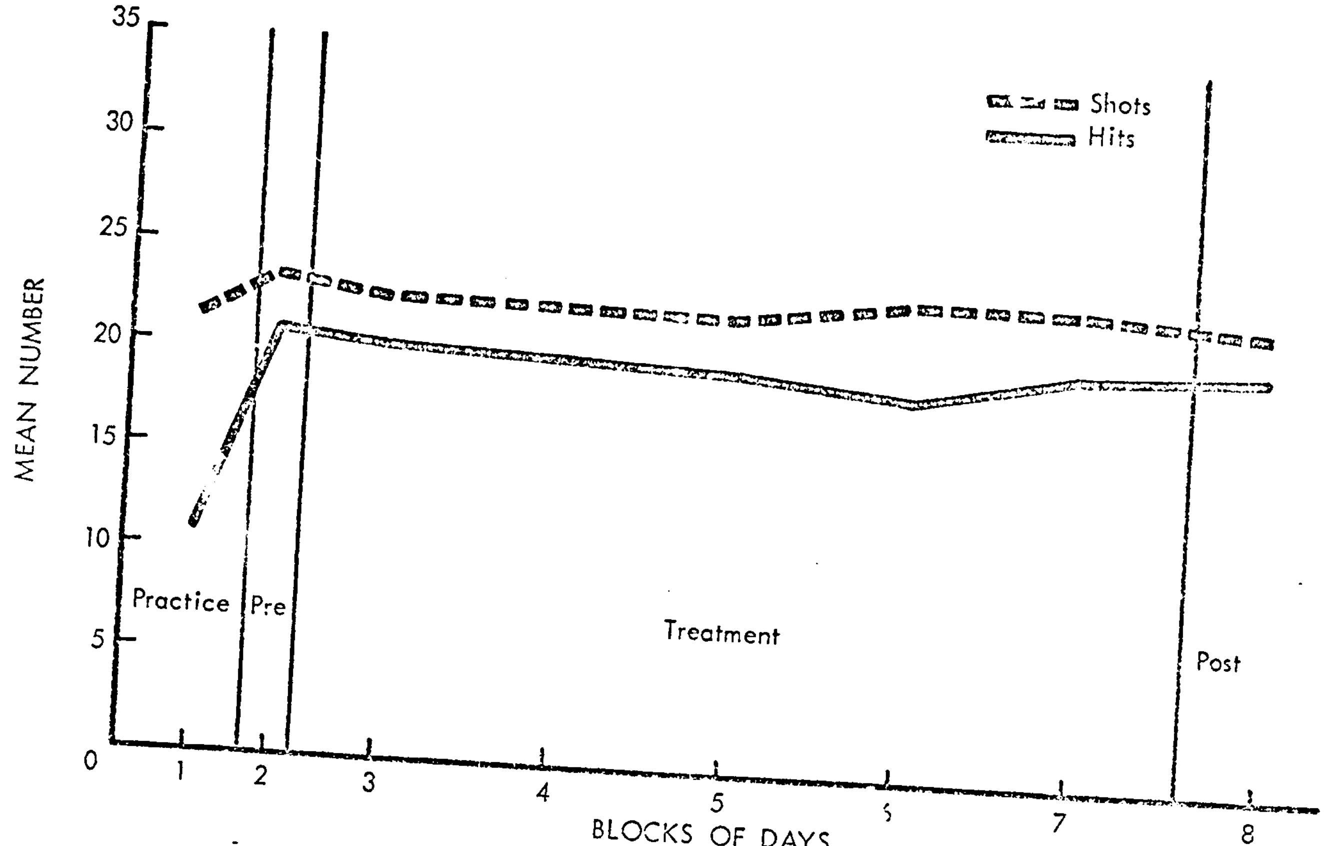

Fig. 17. Mean number of shots and hits for Task B for S 7 only during practice, pretreatment, treatment, and posttreatment periods. Blocks of days represent data averaged for five consecutive days.

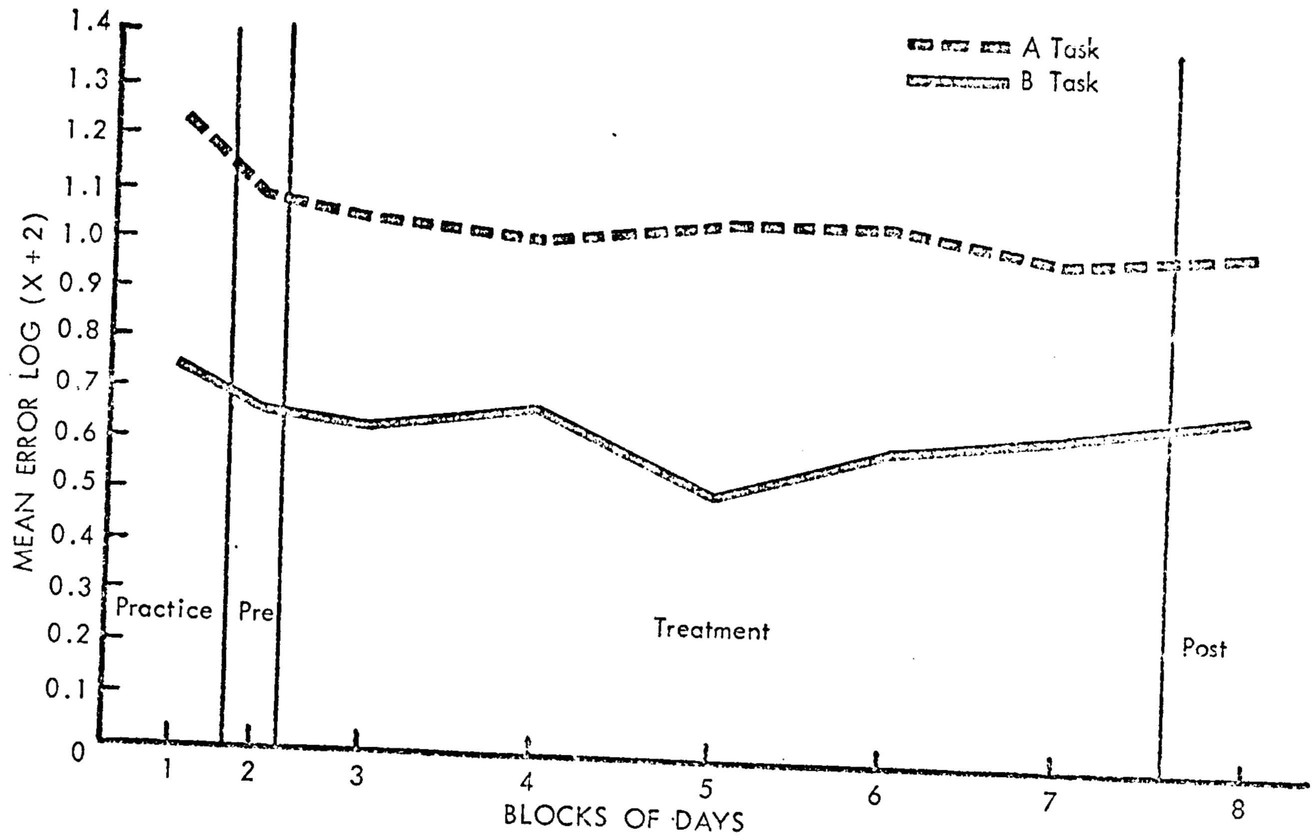

Fig. 18. Mean error log $(X + 2)$ of Tasks A and B during practice, pretreatment, treatment, and posttreatment periods. Blocks of days represent data averaged for five consecutive days.

Table 16

Analysis of Variance for Task B Mean Log (X+2) Error Scores

Source of Variation	SS	df	MS	F
Between Subjects (subjects)	10.7216	5		
A	0.0022	1	0.0022	*
Subjects within groups	10.7194	4	2.6798	
Within Subjects (blocks of days)	11.4094	78		
B	1.6168	6	0.2694	2.0875
AB	0.4737	6	0.0789	0.6111
B X subjects within groups	3.2352	24	0.1348	
C (trials)	0.0010	1	0.0010	0.0070
AC	0.1771	1	0.1771	1.0700
C X subjects within groups	0.6620	4	0.1655	
BC	0.9827	6	0.1637	1.2680
ABC	1.4439	6	0.2406	1.5890
BC X subjects within groups	2.8170	24	0.1173	
MS error within (pooled)		52	0.1291	

*All F ratios, $p > .10$

accuracy of firing, and rate of error (Task B) associated with daily Cobalt-60 irradiation (under the conditions of this study), with average dose rates to the tumor of 42 to 60 rads/min. and total daily tissue doses of 180 to 200 rads.

Discussion

The complex motor coordination task included an easy (A) and difficult (B) task. The S's performance was measured within 5-10 min. following Cobalt-60 irradiation of relatively generous volumes (pelvis, for the most part). No reliable changes in rate, accuracy, or errors of performance were found when the six weeks of treatment were compared to pre and posttreatment performance.

These findings are comparable to the results obtained by Payne (1958). He reported two postirradiation studies of complex motor performance in adult males who were in the advanced stages of neoplastic disease. In the first study, the Ss were treated either with whole-body irradiation (5,25, 50 R) delivered in one dose, or with five equal dose increments separated by intervals of 1 hr. Exposure intensity was related to the severity of illness. Performance was assessed over a 10-day period. In his second study, single doses, ranging from 0 through 200 R in 25 R steps, were sampled. He did not find psychomotor effects or radiation impairment in either of the two studies.

The patients in the present study, as contrasted to Payne (1958), did not exhibit symptoms of radiation illness; hence, reduction in performance was not expected. The patients were in relatively good physical condition, and quite well-motivated to achieve a high level of performance. Thus, any transient irradiation effects on performance (5-10 min. after treatment) might be obscured or compensated for by the motivation of the patient and the complexity of the task.

It was felt that further study, using this measure of performance, was not likely to yield additional pertinent information; therefore, the target shooting task has been discontinued as a method of study.

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APPENDIX A

Medical Summary of the 12 Patients

Participating in the Study

S 1 Case 1. A 45-year-old white male referred for postoperative radiotherapy after superficial right parotidectomy for a lymphosarcoma. This lesion was subsequently shown to be associated with a nasopharyngeal primary and the diagnosis of lymphosarcoma, primary in the nasopharynx, with metastasis to the parotid region was made. Patient was treated from 6-6-66 to 7-18-66 with Cobalt-60 at an SSD of 90 cm. Opposing 10 x 10 cm fields were directed at the right parotid and nasopharynx and which incidentally included a portion of the brain. Estimated tissue exposure (delivered) 4900R; estimated tissue dose (absorbed) 4700 rads. There was no evidence of disease at conclusion of radiotherapy. At the last follow-up examination on 10-30-68 the patient was in good condition with no evidence of the presenting disease.

S 2 Case 2. A 70-year-old white male with nasopharyngeal lymphosarcoma and massive left cervical and superclavicular adenopathy and another focus of lymphosarcoma at base of tongue. Treated from 12-27-66 to 3-3-67 (with a rest interval from 1-24-67 to 2-13-67) with Cobalt-60 at an SSD of 90 cm. Opposing 9 x 11 cm nasopharyngeal fields were employed. The estimated tissue exposure (delivered) was 5100R; the estimated tissue dose (absorbed) was 4900 rads.

S 3 Case 3. Additional irradiation was later directed at the low neck and also to the inguinofemoral and paraaortic areas, which subsequently developed evidence of disease.

At conclusion of the latter therapy on 6-9-67, the patient was going slowly downhill and he expired on 10-29-67.

S 5 Case 5. A 54-year-old white male with squamous cell carcinoma of laryngeal true cords, stage I. Irradiated from 8-11-66 to 9-27-66 with Cobalt-60 at SSD 90 cm through opposing 5 x 5 fields. Estimated tissue exposure (delivered) 6300R; estimated tissue dose (absorbed) 6000 rads. At conclusion of irradiation there was a brisk reaction. Subsequent course was unsatisfactory and patient had a total laryngectomy on 4-28-67 for residual carcinoma. When last seen on 1-15-68 patient was doing well with no evidence of residual disease.

S 6 Case 6. A 66-year-old white male with squamous cell carcinoma larynx, stage II, treated from 4-8-66 to 5-23-66 with Cobalt-60 at SSD 90 cm. Estimated tissue exposure (delivered) 6500R; estimated tissue dose (absorbed) 6200 rads. At conclusion of irradiation, reaction was brisk. When last seen on 1-31-69 patient was in good condition with no evidence of residual disease.

S 7 Case 7. A 22-year-old white male who had had a craniotomy elsewhere with excision of an oligodendroglioma (apparently limited to the region of the left rolandic fissure) in November 1966. However,, he came to us in April 1968 with the symptoms of residual tumor, manifested particularly by an increasing right hemaparesis. The sensorium, however, was quite clear, and the lesion was felt to be still rather limited

in extent. He was treated from 4-4-68 to 5-29-68 with Cobalt-60, SSD 90 cm. Opposing 10 x 12 fields were centered on the rolandic fissure. Estimated tissue exposure (delivered) 5900R; estimated tissue dose (absorbed) 5600 rads. Patient tolerated therapy well. At conclusion of treatment there was still some residual weakness of the right lower extremity but the previously weak right upper extremity was essentially normal. Sensorium was clear. When last seen on 1-23-69 patient was essentially well and walked easily in spite of minimal residual weakness of the right leg.

S 8 Case 8. A 59-year-old white male with a well differentiated squamous cell carcinoma of the right retromolar area, stage IV, extending anteriorly along the floor of the mouth and superiorly and medially to involve the anterior tonsillar pillar and tonsil. There was, in addition, a 4 cm right cervical adenopathy. The patient was treated from 3-19-68 to 5-3-68 with Cobalt-60 at SSD 90 cm. Opposing 10 x 12.5 fields were directed at the extensive retromolar lesion and incidentally irradiated a portion of the normal brain. Estimated tissue exposure (delivered) 6800R; estimated tissue dose (absorbed) 6500 rads. The patient tolerated therapy well. The original nodal mass was no longer palpable. The massive ulcerated tumor regressed but a residual 2 cm excavation remained in the retromolar area. Eventually this proved to be the site of residual disease. After a positive biopsy a right hemimandibulectom , hemiglossectomy, and cervical lymphodectomy were performed on

11-13-68. When last seen on 1-21-69 there was some evidence of persistent disease.

S 9 Case 9. A 44-year-old Negro male with squamous cell carcinoma of the nasopharynx and bilateral cervical metastasis. Treated from 4-17-68 to 6-7-68 with Cobalt-60 at 90 cm SSD. Specially contoured 13 x 16 opposing fields were directed at the nasopharynx and associated adenopathy, and incidentally included a portion of the apparently normal brain. Estimated tissue exposure (delivered) 6300R; estimated tissue dose (absorbed) 6000 rads. Patient tolerated radiotherapy well. At conclusion of therapy the cervical adenopathy was no longer palpable and the nasopharyngeal primary lesion had apparently regressed. However, on the patient's last return 2-5-69, there was marked hepatomegaly (obviously metastatic), and the patient appeared to be premoribund.

S 10 Case 10. A 72-year-old white male with grade IV transitional cell carcinoma of the urinary bladder and extra-vesical spread presumably confined to the pelvis (stage IV). Treated from 1-11-68 to 2-23-68 with Cobalt-60 at SAD 80 cm through one anterior 15 x 15 cm and two posterior oblique 10 x 15 cm fields directed at the bladder. All three fields were irradiated each day to a total of 200R (tis.) at the axis. Estimated tissue exposure (delivered) 6200R; estimated tissue dose (absorbed) 6000 rads. Morbidity was minimal during radio-therapy; however, palliation was short-lived. When seen on 5-15-68 the patient was obviously going downhill, with

bilateral ureteral obstruction and considerable back pain. He expired on 6-16-68.

S 11 Case 11. A 51-year-old white male with Grade IV transitional cell carcinoma of bladder obstructing the left ureter. Left nephroureterectomy with segmental resection of bladder was done on 12-18-67. Treated from 1-8-68 to 2-21-68 with Cobalt-60 at SAD 80 cm through one anterior 15 x 12 cm field and two posterior oblique 10 x 12 cm fields directed at the bladder. All three fields were irradiated each day to a total of 200R (tis.) at the axis. Estimated tissue exposure (delivered) 6500R; estimated tissue dose (absorbed) 6200 rads. Patient tolerated radiotherapy fairly well. Outlook was, of course, poor. Patient eventually developed severe neuritic pain and expired on October 3, 1968.

S 12 Case 12. A 51-year-old white male with a rare anaplastic adenocarcinoma apparently primary in the urinary bladder and invading the muscle (stage III). However, general condition was good and sensorium was clear. Treated from 11-8-67 to 1-22-68 with Cobalt-60 at SAD 80 cm through one anterior 15 x 10 cm field and two posterior oblique 10 x 10 cm fields directed at the bladder. All three fields were irradiated each day to a total of 180R (tis.) at the axis. Estimated tissue exposure (delivered) 6800R; estimated tissue dose (absorbed) 6500 rads. At the conclusion of therapy there was no longer any hematuria. Therapy was well tolerated. When last seen on 1-3-69 there was some minor evidence of proctitis

S 13 Case 13. A 49-year-old Negro male with multicentric, grade IV, transitional cell carcinoma of the bladder (Stage II) with involvement of the right lateral wall, dome, vesicle neck and floor. No clear evidence of muscle invasion, however. Treated from 2-28-68 to 4-12-68 with Cobalt-60 at SAD 80 cm through one anterior 15 x 12 cm field and two 10 x 12 cm posterior oblique fields directed at the bladder. All three fields were irradiated each day to a total of 200R (tis.) at the axis. Estimated tissue exposure (delivered) 6600R; estimated tissue dose (absorbed) 6300 rads. Morbidity was minimal during the radiotherapy. When last seen on 1-30-69 there was no dysuria frequency, pain, or diarrhea and the patient felt essentially well.

APPENDIX B

RADIATION DOSIMETRY

I. Introduction

A dosimetric study was performed for each patient by reproducing the treatment fields for each patient on an Alderson-Rando Phantom in which the exposure at 131 points in the head and neck was measured using Lithium Fluoride (LiF) dosimeters. Replicate measurements were made for each patient and average values were determined.

II. Equipment

A. Phantoms

The phantoms used were Alderson-Rando Standard Man phantoms, serial numbers 110 and 139. (Number 139 was borrowed from The Armed Forces Radiobiological Research Institute and used from March through May of 1968. Number 110 was borrowed from the UCLA Medical School and used from August 1968 through February 1969.) Figures 1B and 2B show photographs of the phantom; Figures 5, 6, and 7 (pages 18, 19,20) show the exposure geometry and the location of the 131 points at which exposure was measured. Both phantoms had been manufactured with a standard hole grid, i.e., each of the components contained an array of holes which were 5 mm. in diam. and were spaced on a 3 cm. grid. In order to accomodate the 1.0 mm. diam. LiF rods and eliminate any air spaces preventing secondary particle build-up for Cobalt-60 dosimetry, the 55 mm. holes were fitted with polyethylene tubing as shown in Figure 3B.

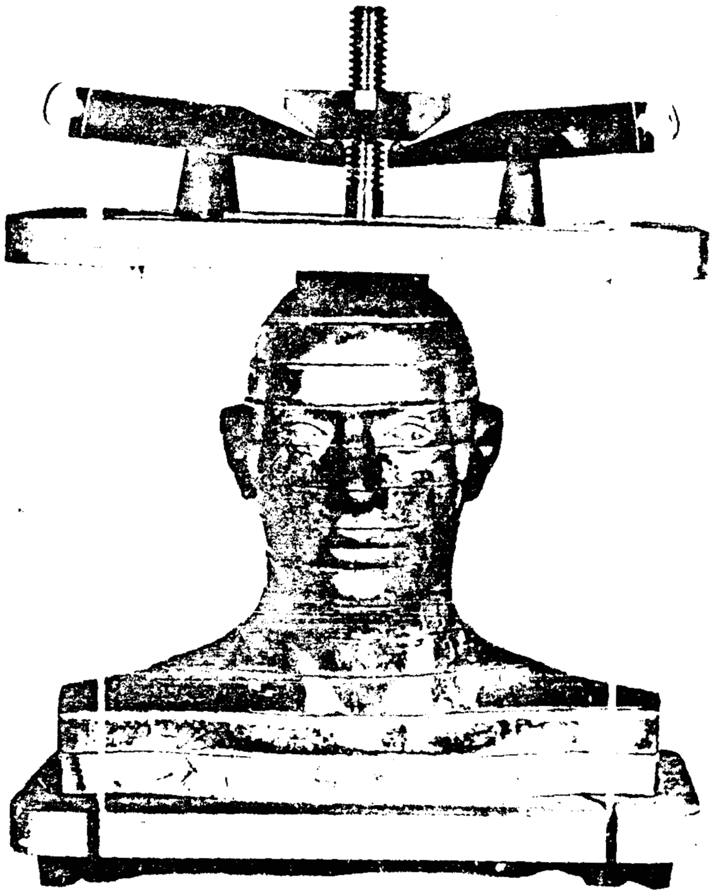


Fig. 1B. Photograph of the Alderson-Rando Phantom, slabs 0 through 12, assembled for exposure.

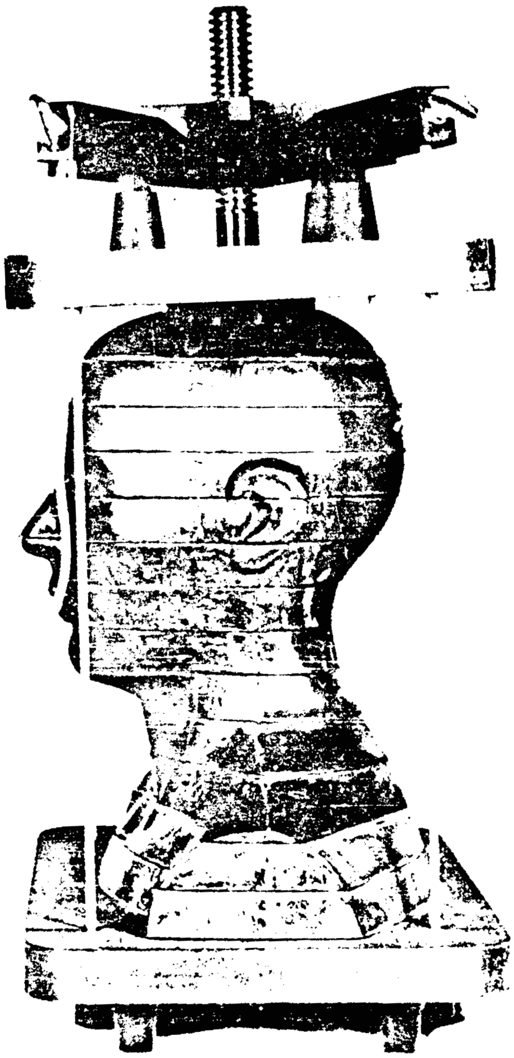


Fig. 2B. Lateral view of the phantom.

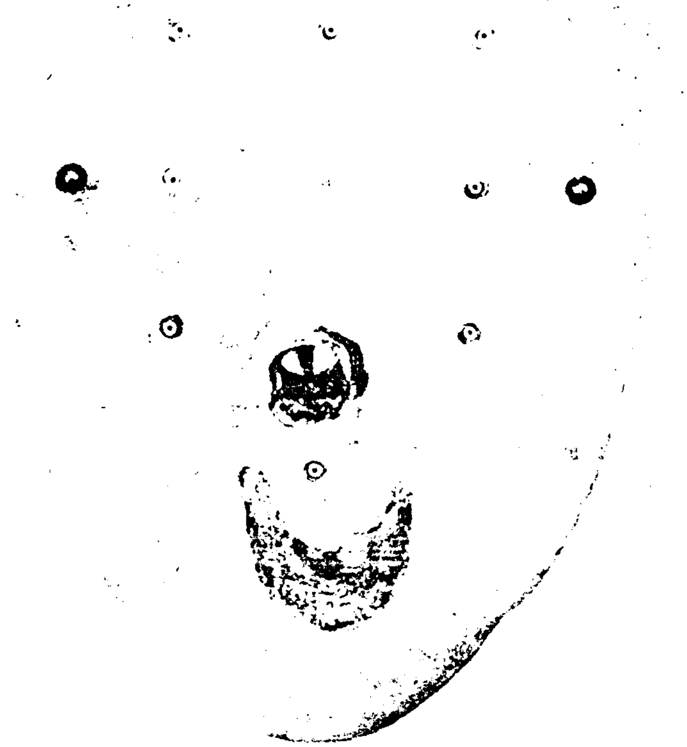


Fig. 3B. Photograph of the superior surface of slab 6 showing the polyethylene tubing used in the holes to accomodate the LiF dosimeters of 1.0 mm. diameter.

B. Dosimeters

Thermoluminescence dosimeters were chosen for their small size. Lithium Fluoride (LiF) was the phosphor used throughout the study. It was chosen for its tissue equivalence and good response to low energy photons (Fowler & Attix, 1966; Cameron, Suntharlingam, & Kenney, 1968). Most of the dosimeters used were measuring scattered radiation, i.e., radiation beyond the primary beam in the phantom. Various forms of LiF were tried: a) glass-encapsulated (E. G. & G., Model No. TL-23); b) Teflon Rods (Con-Rad Microrods 167106); and c) extruded rods (E. G. & G., TL-24 and Harshaw TLD-700 rods). Figures 4B through 9B summarize the measured precision for these various types. The Harshaw rods, which have performed consistently with a precision of $\pm$ 3.5%, were chosen and used throughout the study. The measured dimensions of the Harshaw rods were 1.0 mm. diam. X 6.0 mm. length $\pm$ 0.5 mm. The response to varying exposures was always linear for all types within the range of exposures used in this study, as shown in Figures 10B through 15Ba. Response of LiF is independent of exposure rate to more than 10^8 R/sec. (Fowler & Attix, 1966). The effective atomic number of water (and muscle) is 7.4; the effective atomic number of LiF is 8.1 (Data Sheet 044, Harshaw Chem. Co., 1967).

C. TLD Reader

The Harshaw extruded rod dosimeters were read with an Edgerton, Germeshausen and Grier, Inc. (E. G. & G.). Thermoluminescence Dosimetry System (reader), Model No. TL-3B,

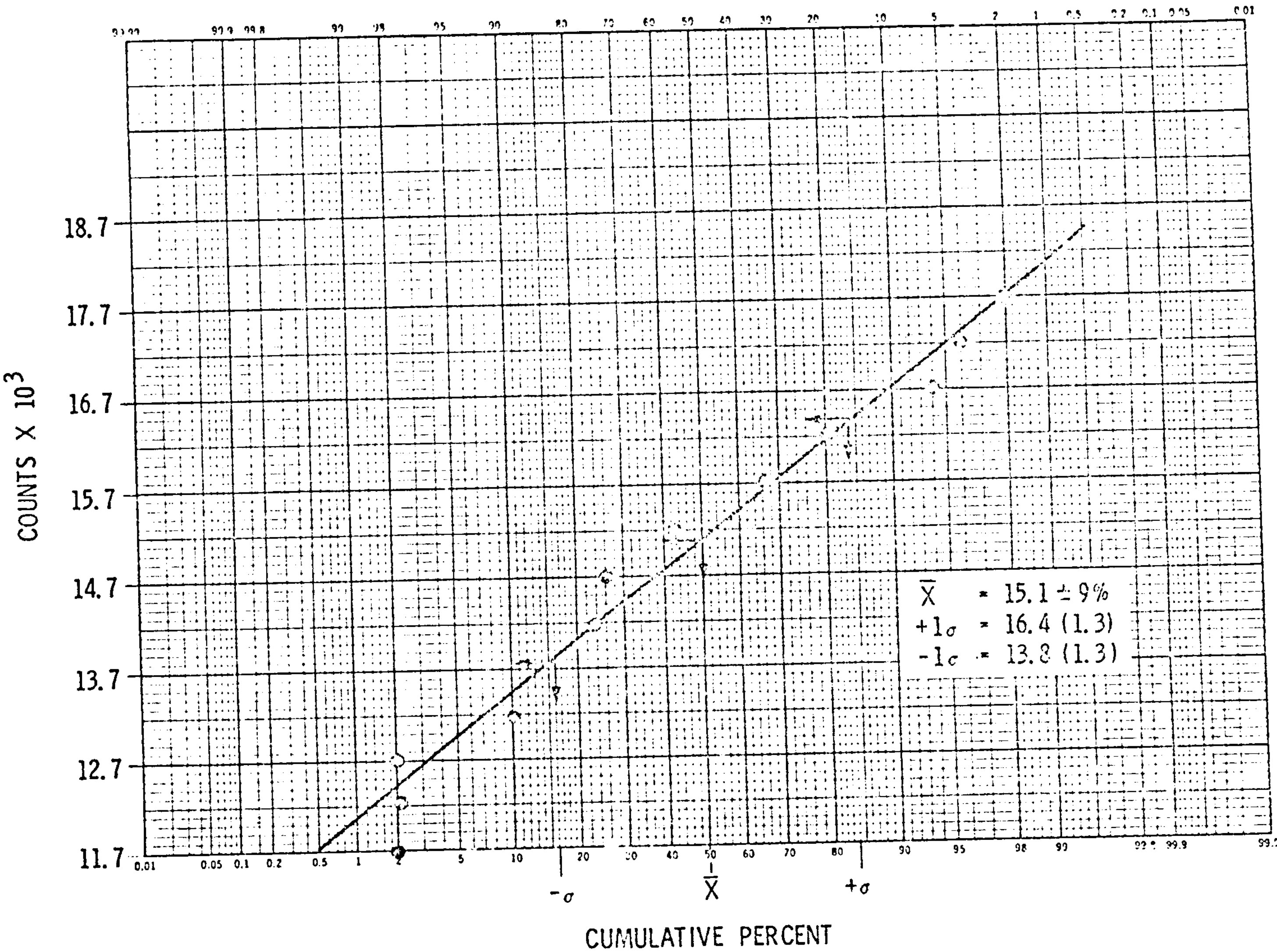


Fig. 4B. Measured precision of EGG dosimeters (Model No. TL-23). Fifty glass-encapsulated, LiF dosimeters were preselected (from 200) for their individual reproducibility. The fifty dosimeters were then exposed simultaneously to 175 R of Cobalt-60 radiation, and subsequently read on the EGG TL-3B reader. The variation within the group was ± 9% at one standard deviation, as indicated (Set D).

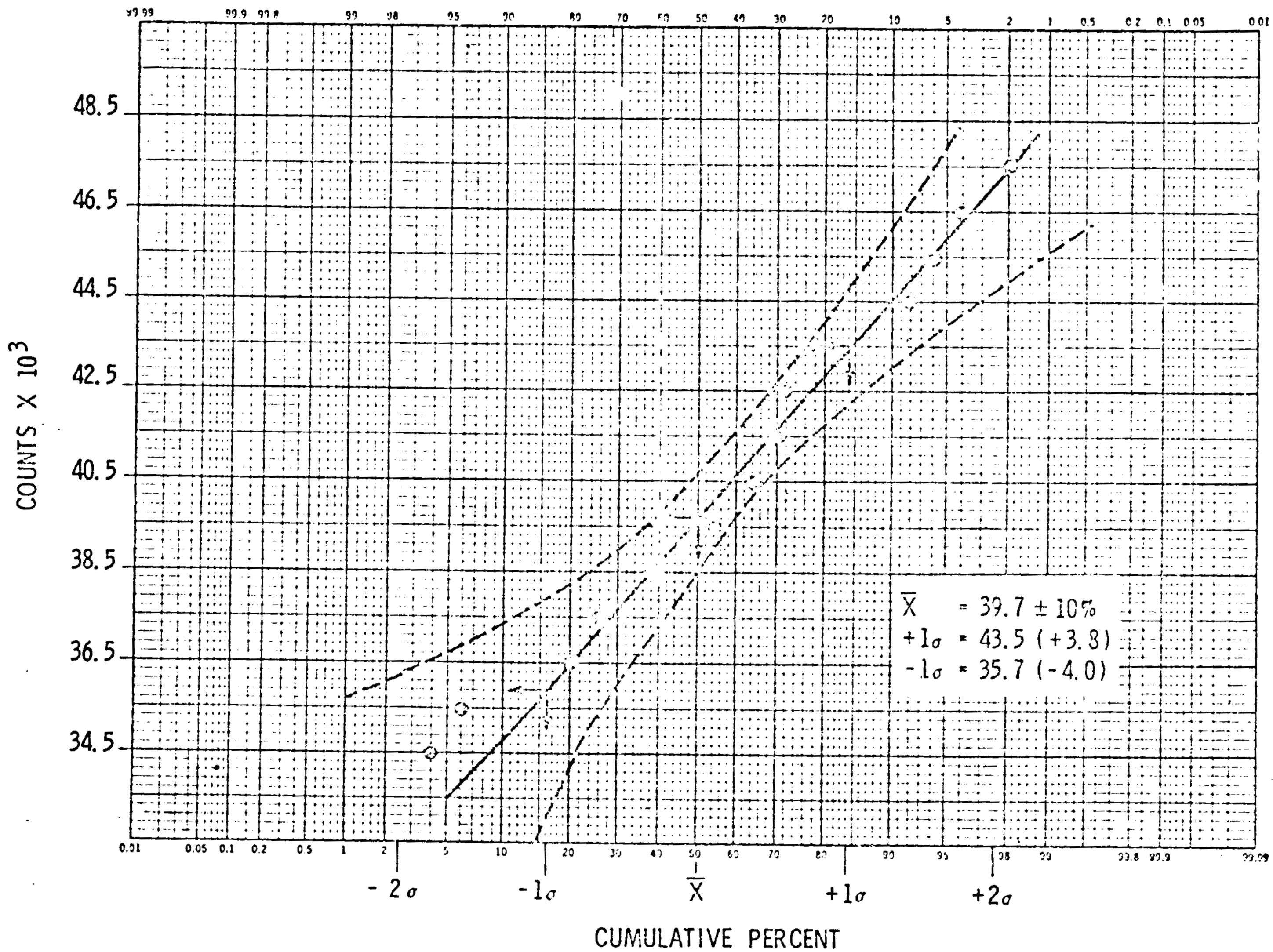


Fig. 5B. Measured precision of Con-Rad dosimeters (Microrods 167106). See caption under Fig. 4B for details. (Set G, 50 dosimeters)

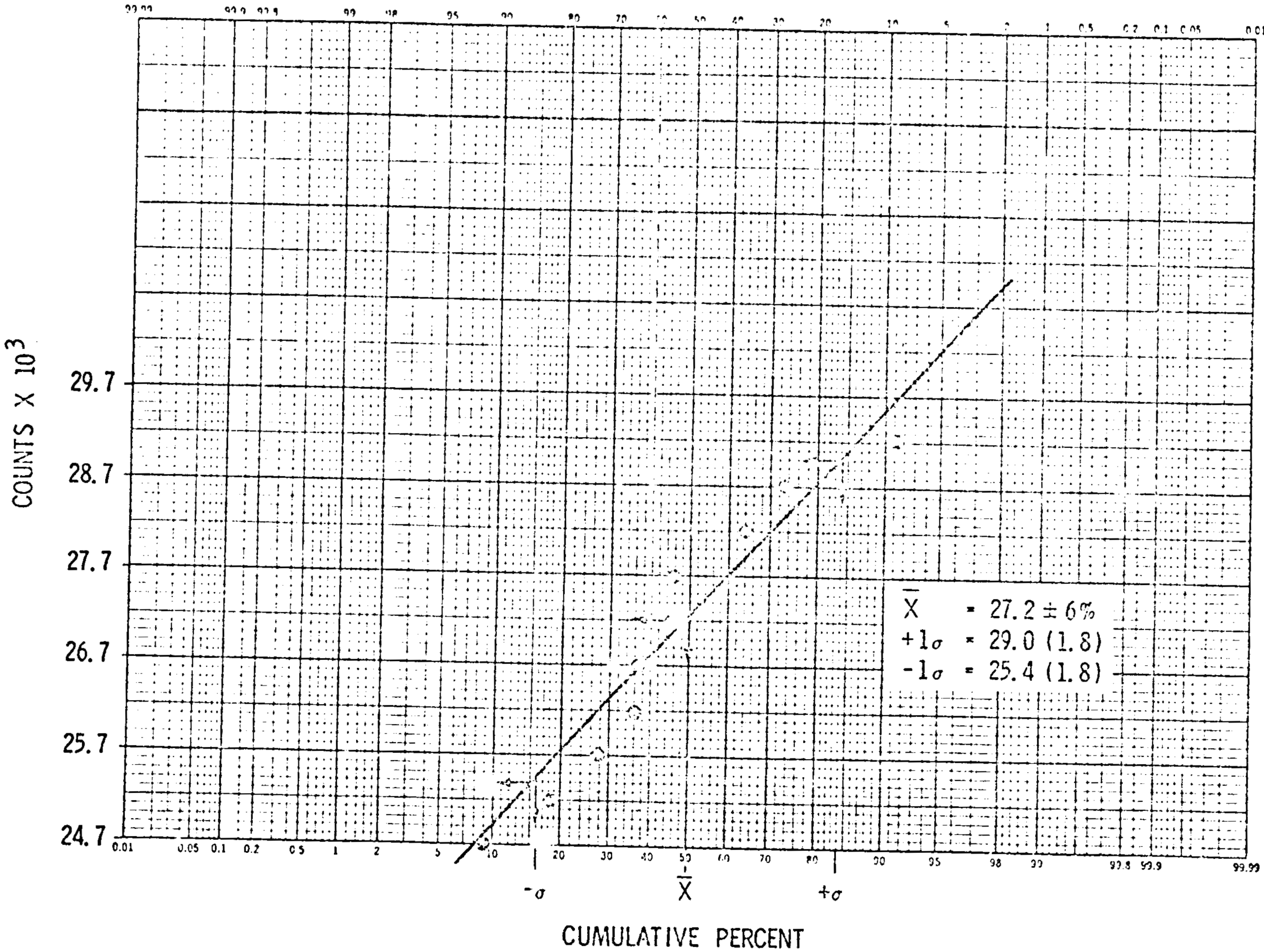


Fig. 6B. Measured precision of EGG dosimeters (extrude LiF, Model No. TL-24).

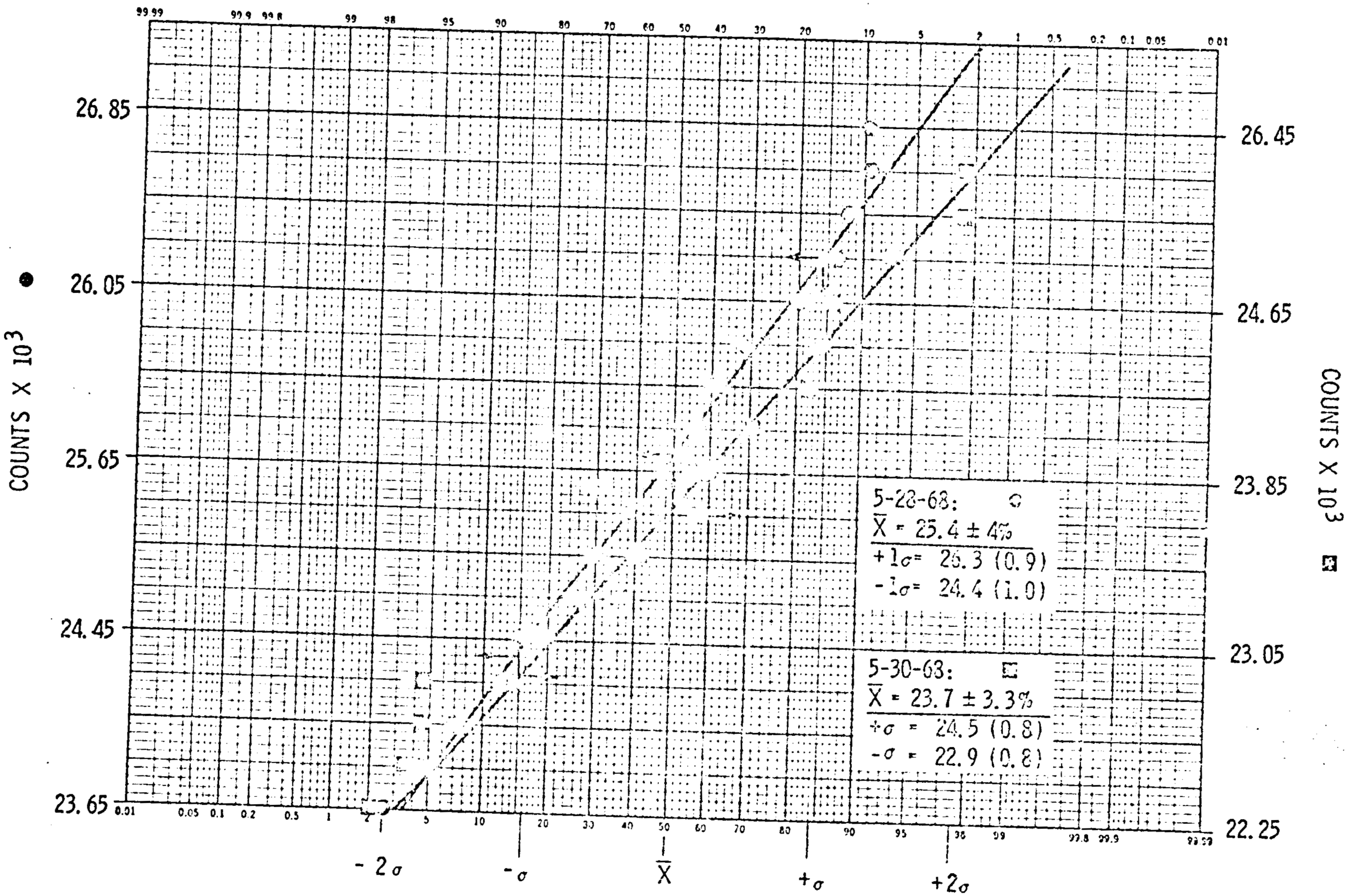


Fig. 7B. Measured precision of Harshaw TLD-200 rods. See caption under Fig. 4B for details. (Set F, 50 dosimeters, not preselected)

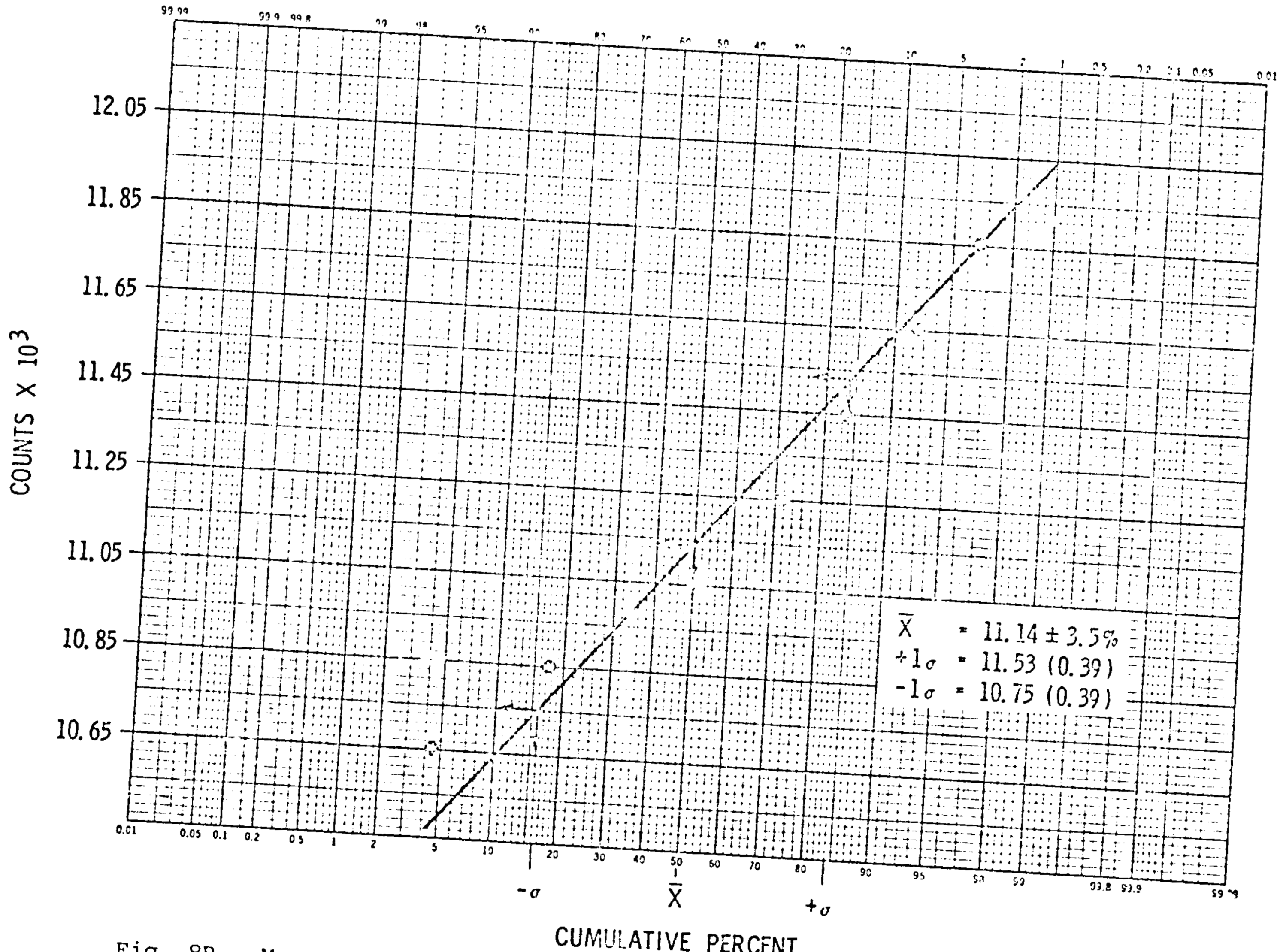


Fig. 8B. Measured precision of Harshaw TLD-700 rods. See caption under Fig. 4B for details. (Set M, 25 dosimeters, not preselected)

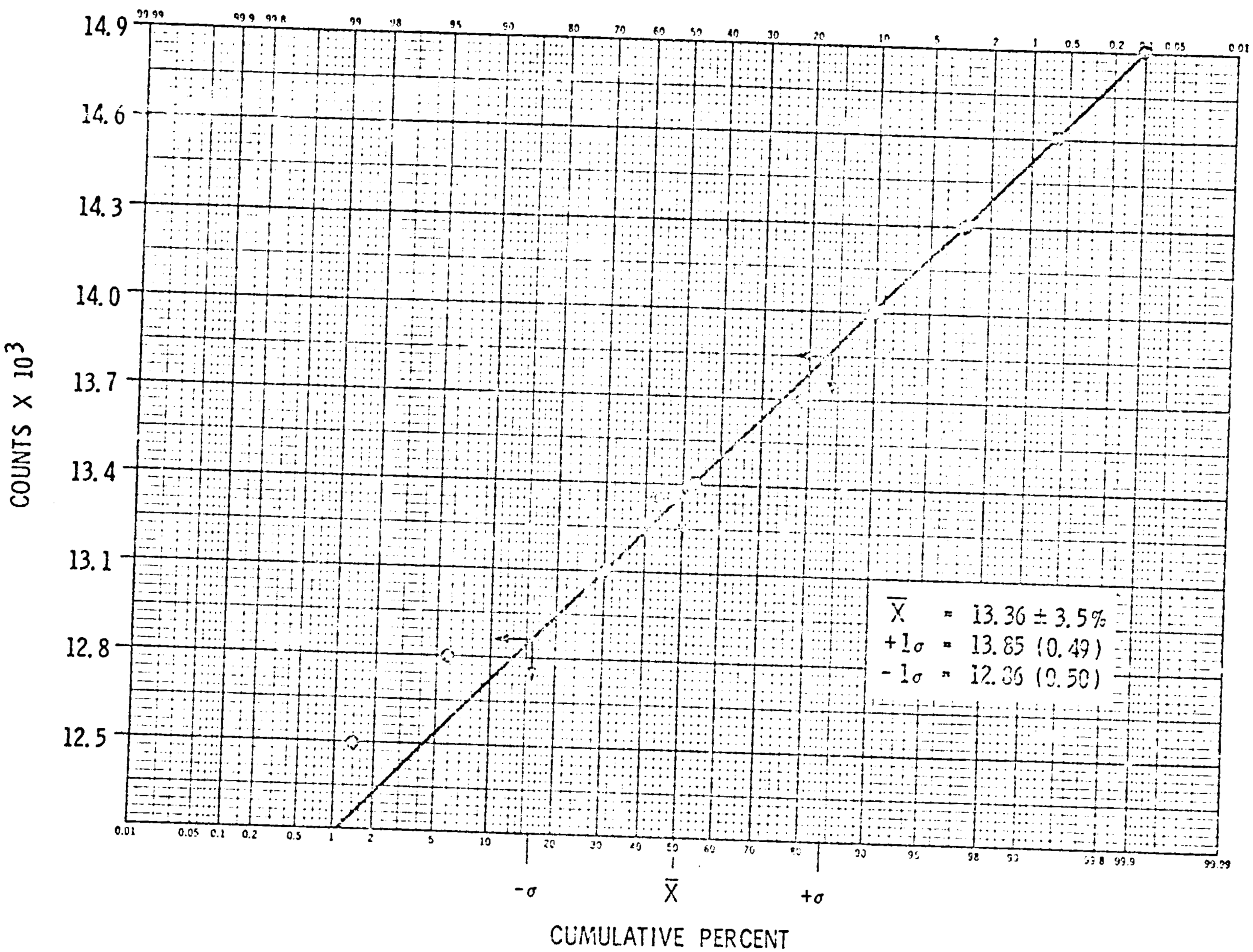


Fig. 9B. Measured precision of Harshaw TLD-700 rods. See caption under Fig. 4B for details. (Set N, 200 dosimeters, not preselected).

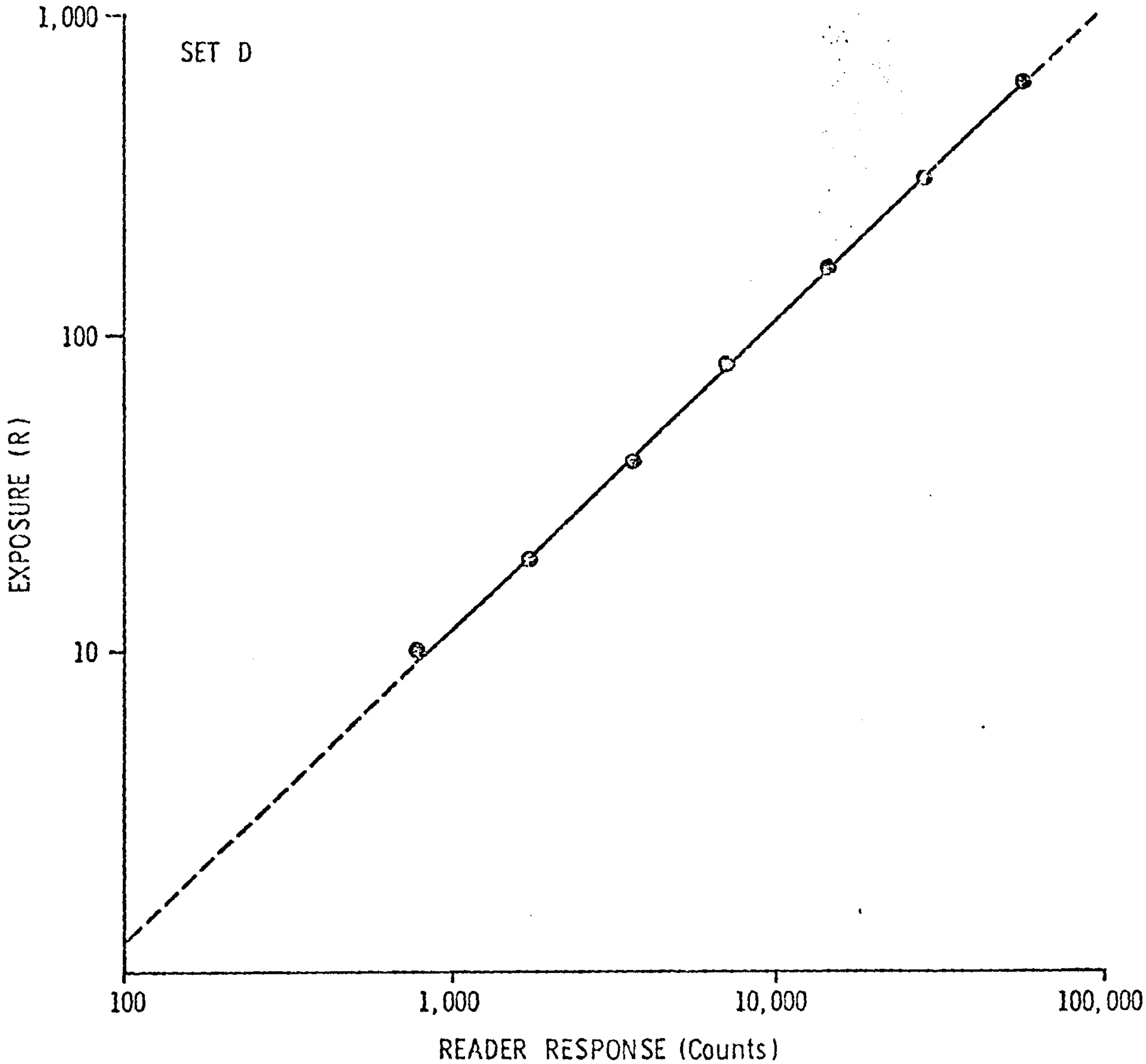


Fig. 10B. Dosimeter response to Cobalt-60 exposure (EGG TL-23).

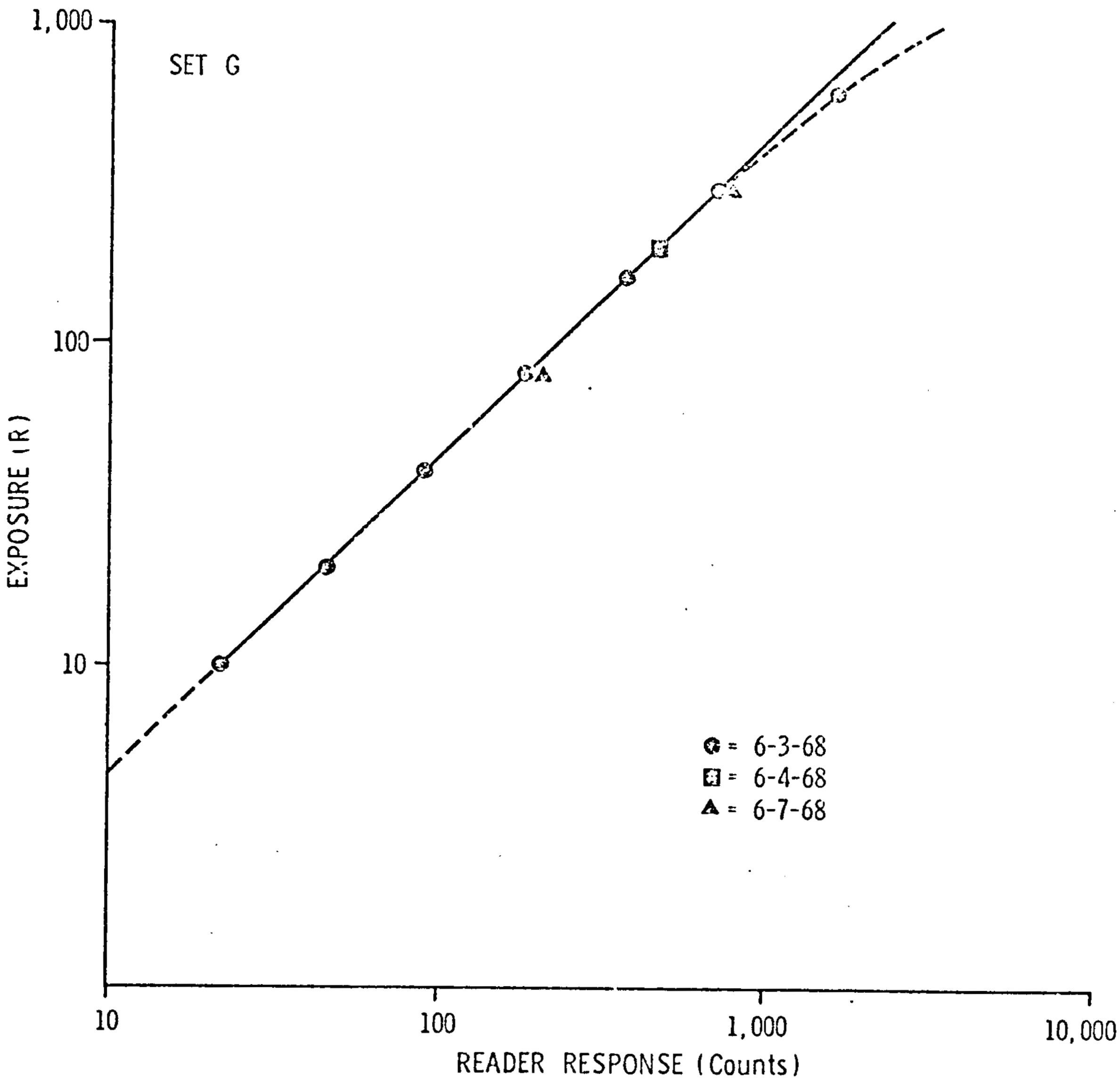


Fig. 11B. Dosimeter response to Cobalt-60 exposure (Con-Rad rods).

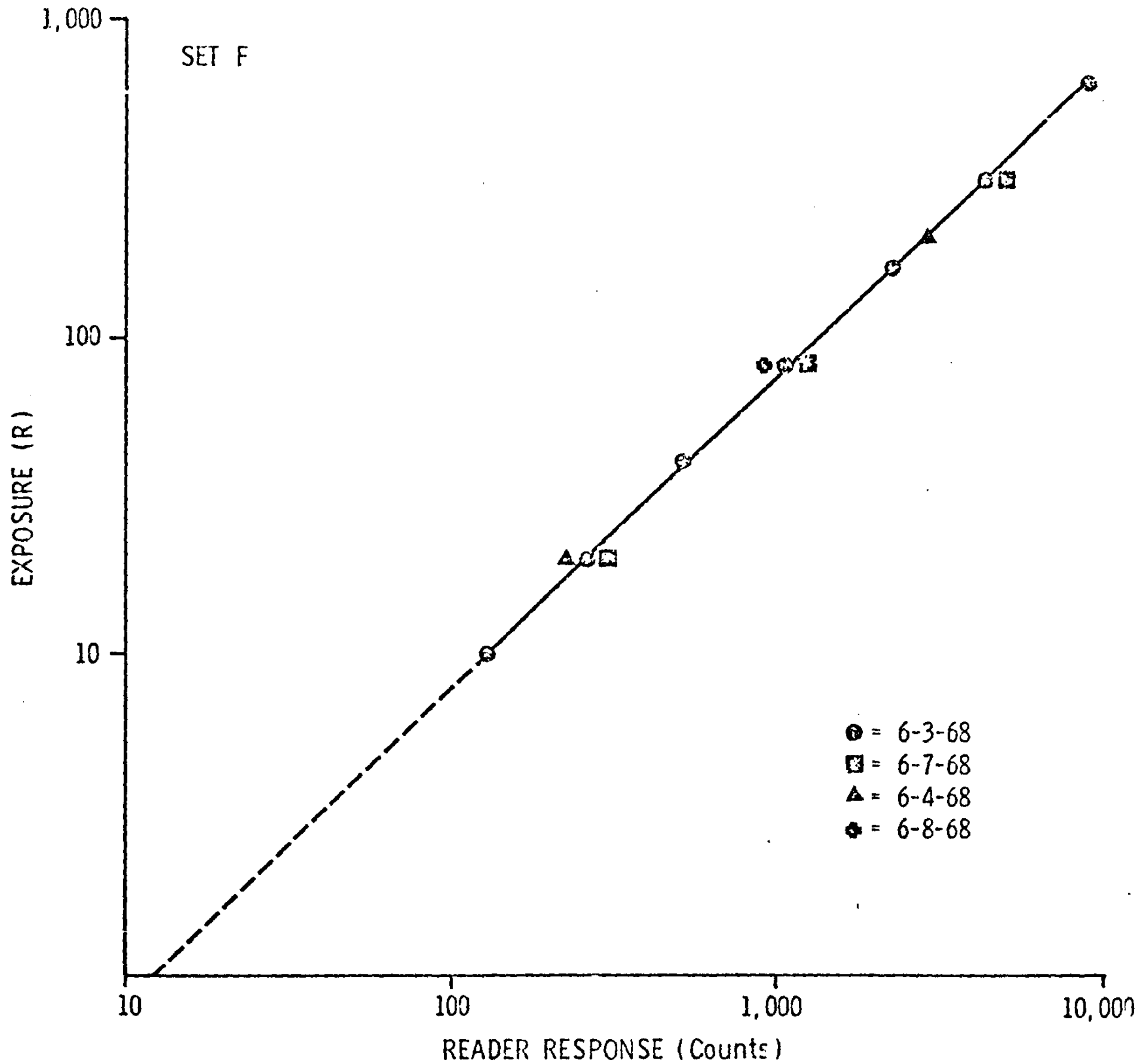


Fig. 12B. Dosimeter response to Cobalt-60 exposure (Harshaw TLD-700 rods).

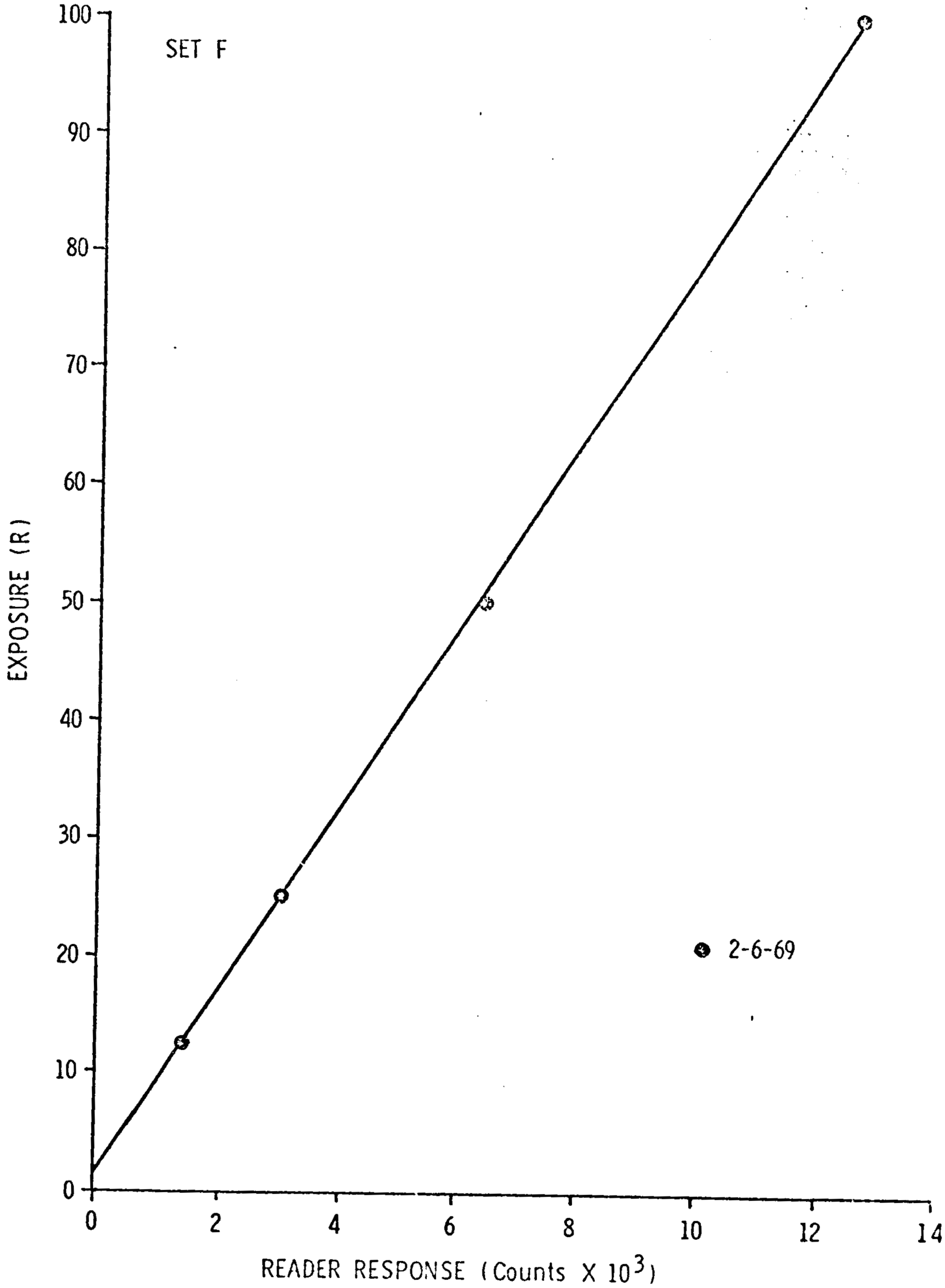


Fig. 13B. Dosimeter response to Cobalt-60 exposure (Harshaw TLD-700 rods).

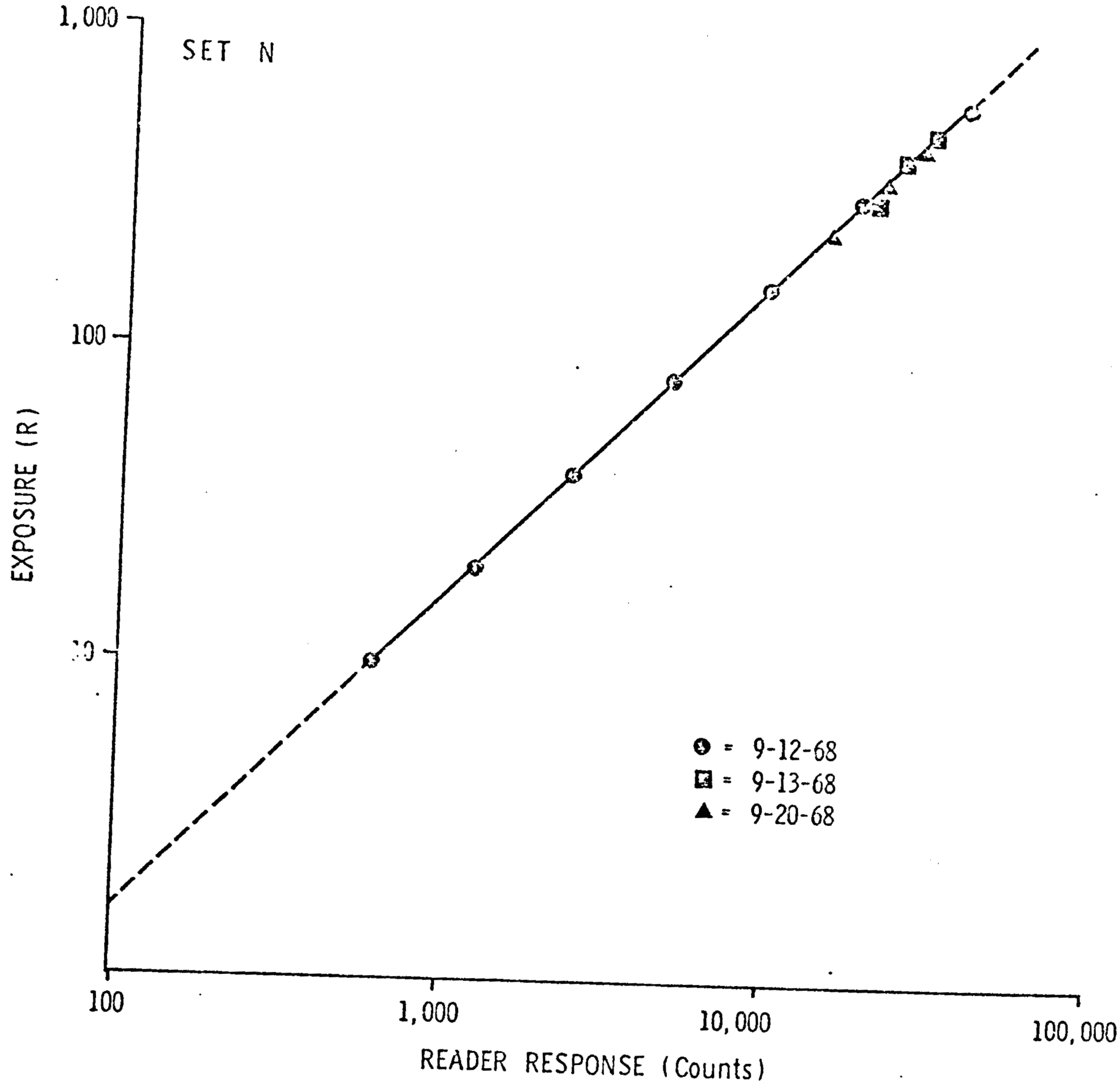


Fig. 14B. Dosimeter response to Cobalt-60 exposure (Harshaw TLD-700 rods).

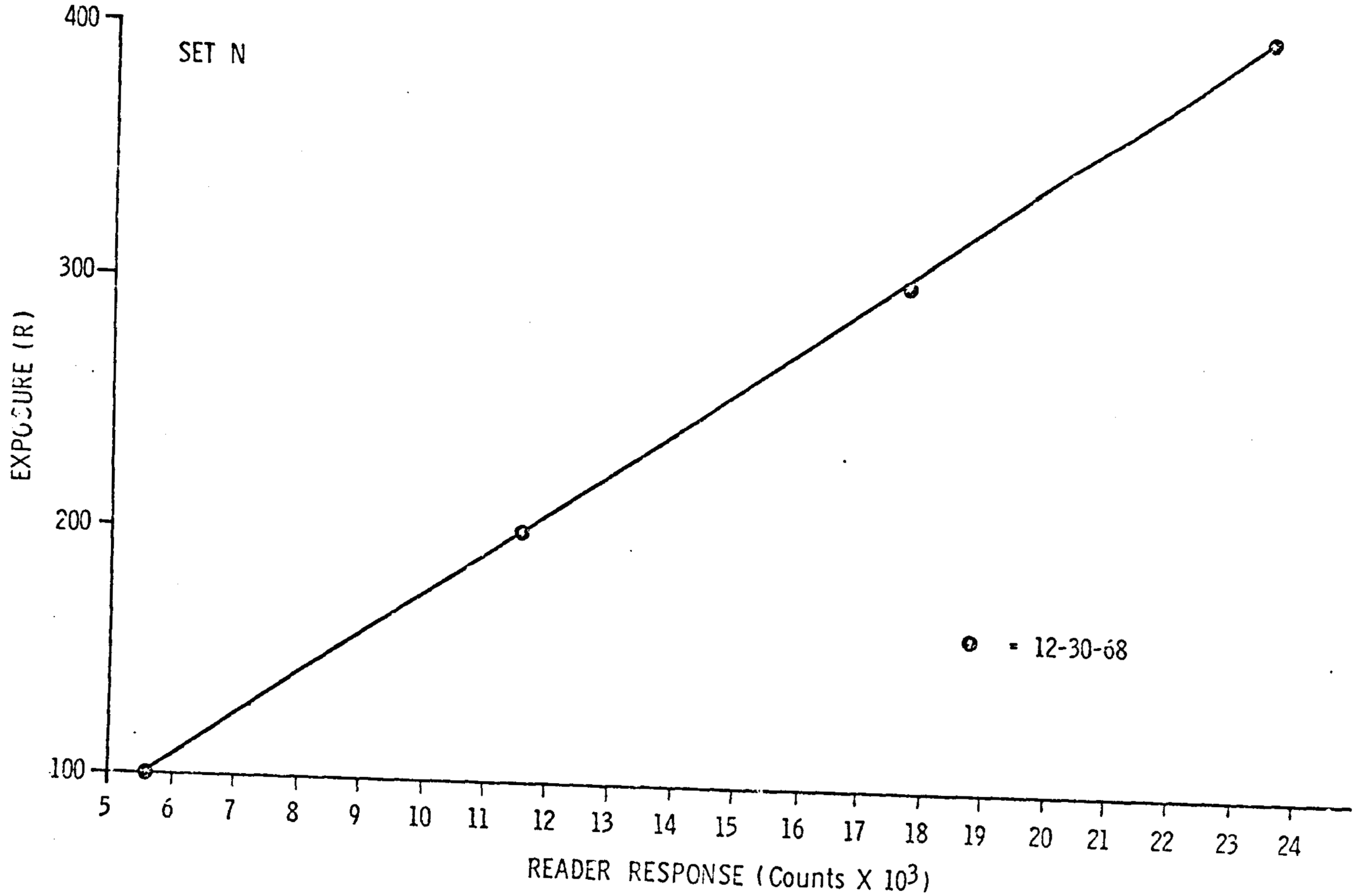


Fig. 15B. Dosimeter response to Cobalt-60 exposure (Harshaw TLD-700 rods).

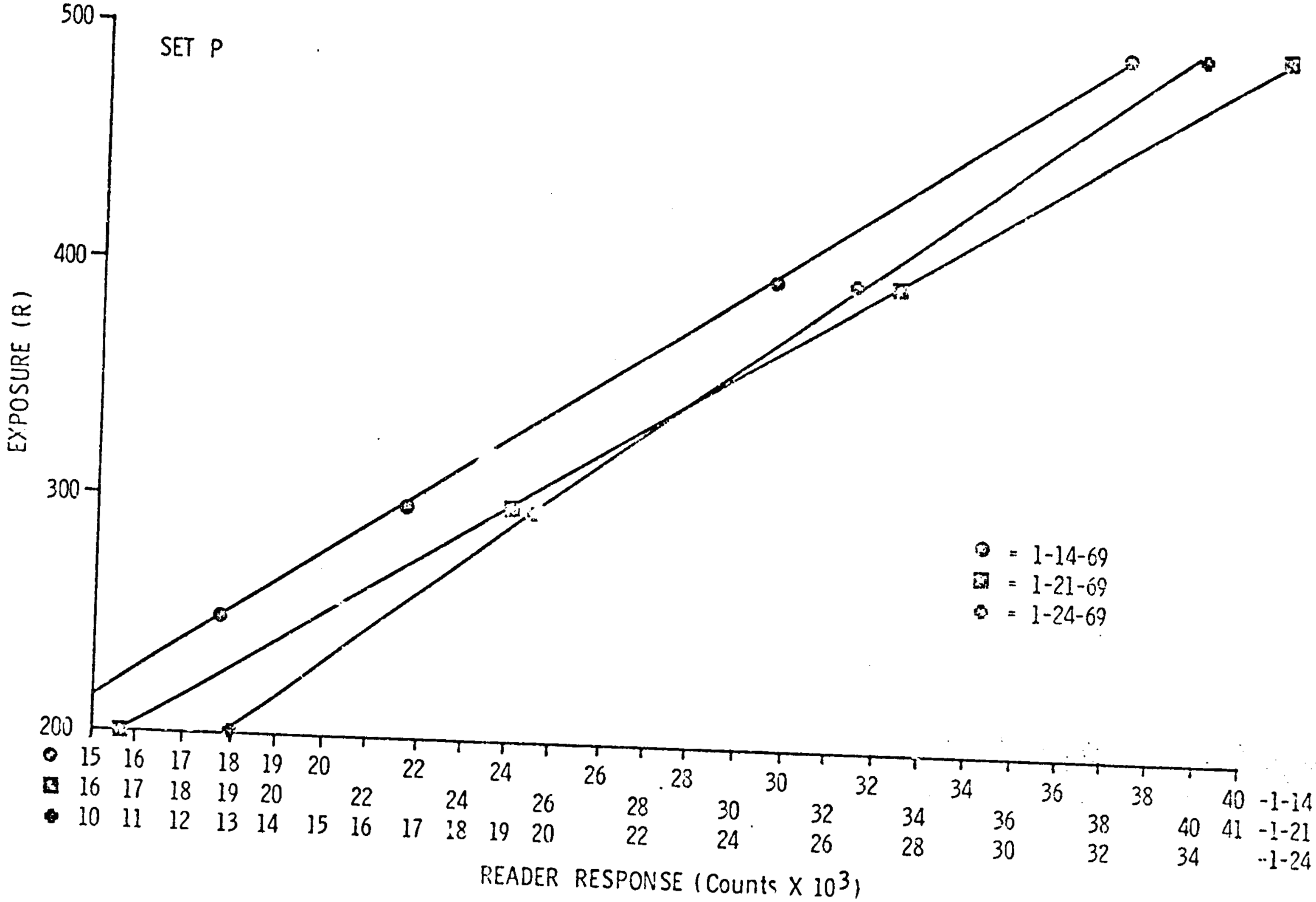


Fig. 15Ba. Dosimeter response to Cobalt-60 exposure (Harshaw TLD-700 rods).

Serial No. 39. The Harshaw rods were positioned and heated in the reader with E. G. & G.'s TL 81B TLD Adaptor. The reader performed well and, with the Harshaw rods, the system operated with a precision of $\pm$ 3.5% as indicated above.

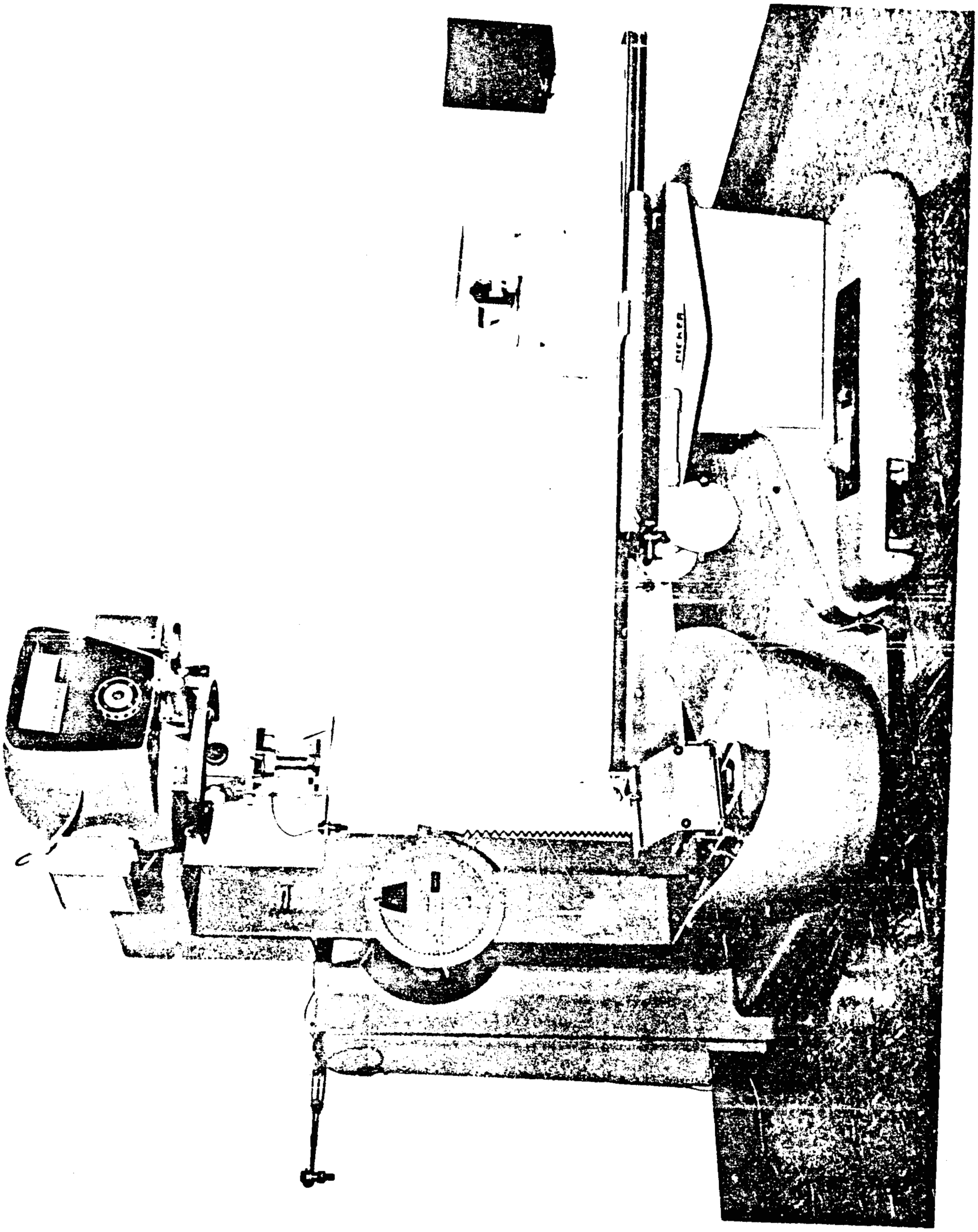
D. Secondary Standard

The secondary standard used for all dosimetry was a Victoreen Condenser R-meter, Model No. 570, SN 1394 with a high energy chamber, Model No. 621, SN 1394. The chamber and electrometer were calibrated by the National Bureau of Standards with Cobalt-60 on May 12, 1967. This chamber and electrometer have been checked quarterly for performance in a Victoreen Radium Standard Model 540B, SN 379, since April, 1966. Over this period of time (April 1966 to February, 1969), the precision of the chamber has varied by $\pm$ 2.4% at 2 standard deviations.

E. The Cobalt-60 Teletherapy Unit

All the dosimetry was performed with a Picker C8M/80 teletherapy unit shown in Figure 16B (Smith et al., 1964). The Cobalt-60 source (2.0 cm. diam.) had an activity of 5260 curies on March 26, 1965. The source contains 27.61 grams of 1 mm. x 1 mm. cobalt pellets. The Unique Half Value Layer of the treatment beam is 9.7 mm Pb. (Figure (17B).

Fig. 16B. The Cobalt-60 Teletherapy machine used in this study. The machine is a Picker X-ray Corporation Model C8M/80.



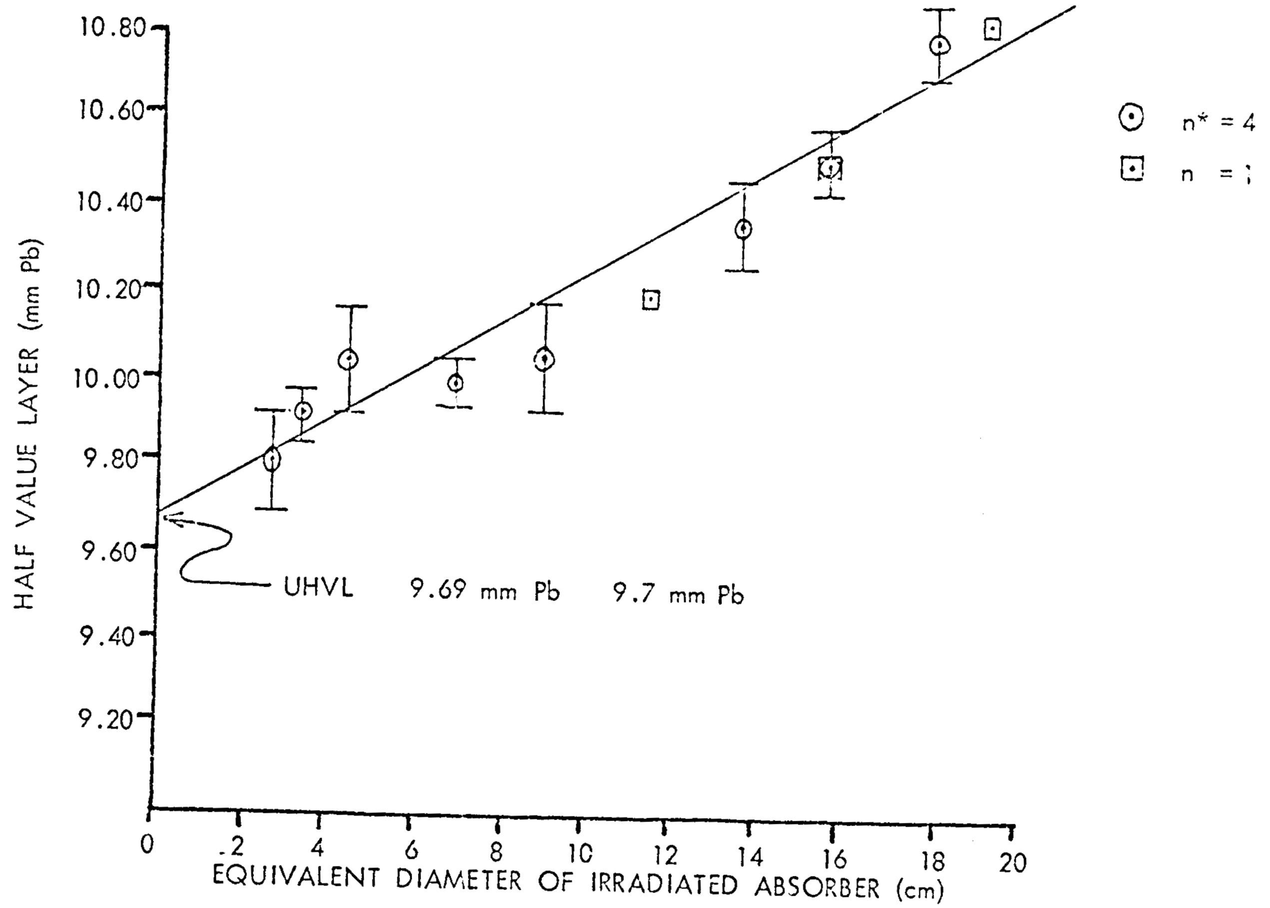


Fig. 17B. The unique half value layer of the treatment beam. Picker C8M/80 Cobalt-60 teletherapy unit 2.0 cm. diam. pellet source; collimator style No. 3347D.

*n = the number of individual HVL determinations

III. Patients

The patients are described in Appendix A.

IV. Procedure

Preceding each exposure, the LiF dosimeters were annealed for 1 hr. at 400° C., cooled in 3 min. to about 100° C., and then further annealed for 2 hrs. at 100° C. Slabs 0 through 12 of the phantom were used for each exposure. The dosimeters were placed in slabs 1 through 10 as shown in Figures 6 7, 3B, and 18B through 24B. Figures 25B and 26B show the size and location of each treatment field used for each patient in the study.

After the dosimeters were placed, the phantom was assembled as shown in Figure 1B and irradiated under the conditions of treatment for each patient (see Figure 5). After the phantom had been exp sed, 36 calibration dosimeters were exposed in four groups of 9 each to four different exposure doses. A typical calibration curve is shown in Figure 15B. Every phantom exposure was accompanied with such a set of calibration exposures.

All dosimeters were then stored for 24 hrs. Before reading (at least 24 hr. after irradiation), all dosimeters were annealed for 10 min. at 100° C. Dosimeters were always handled with tweezers and rinsed with analytical grade methanol. Any dosimeters touched with the hands or otherwise suspected of being dirty were rinsed with warm

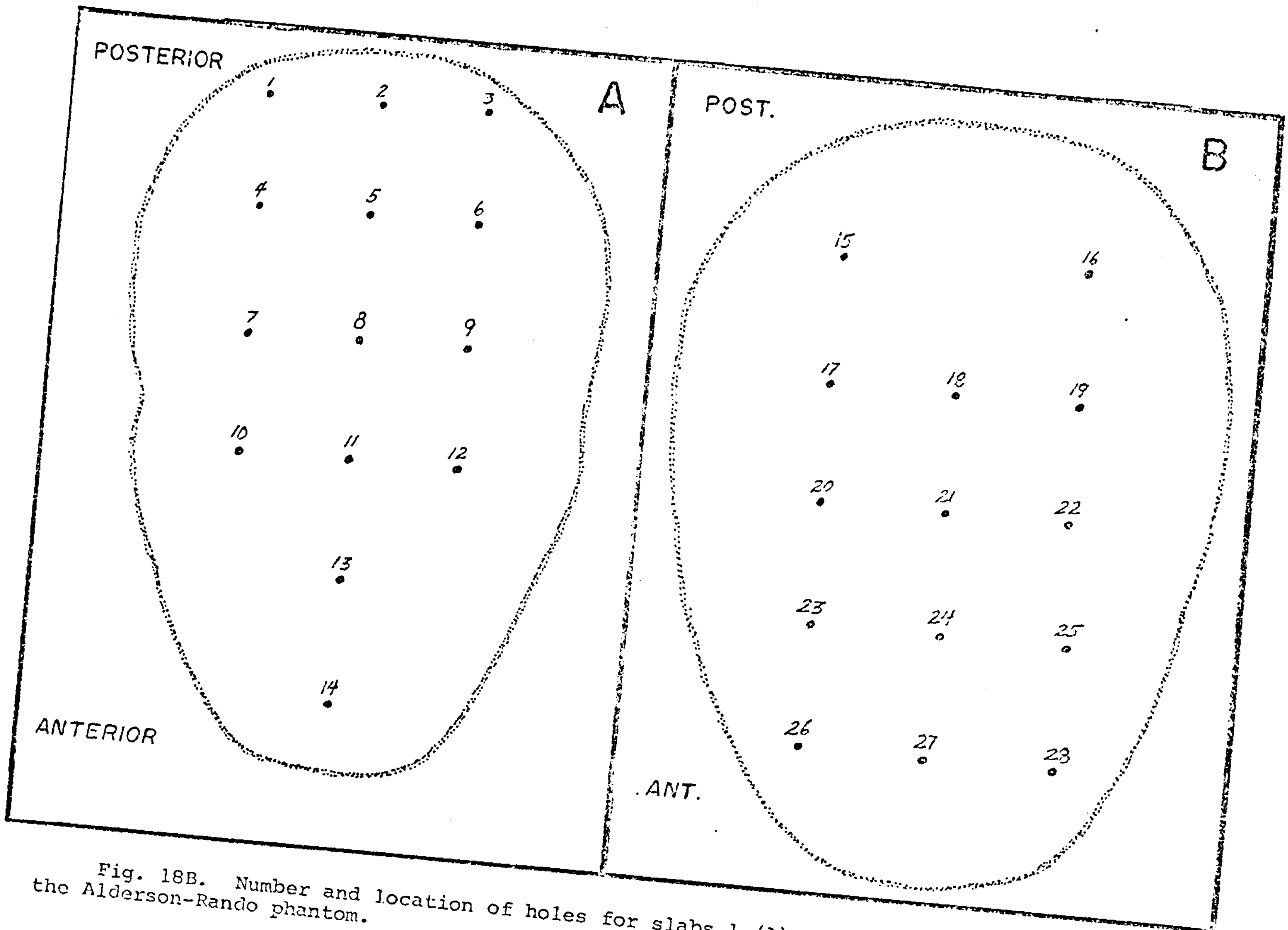


Fig. 18B. Number and location of holes for slabs 1 (A) and 2 (B) superior surfaces the Alderson-Rando phantom.

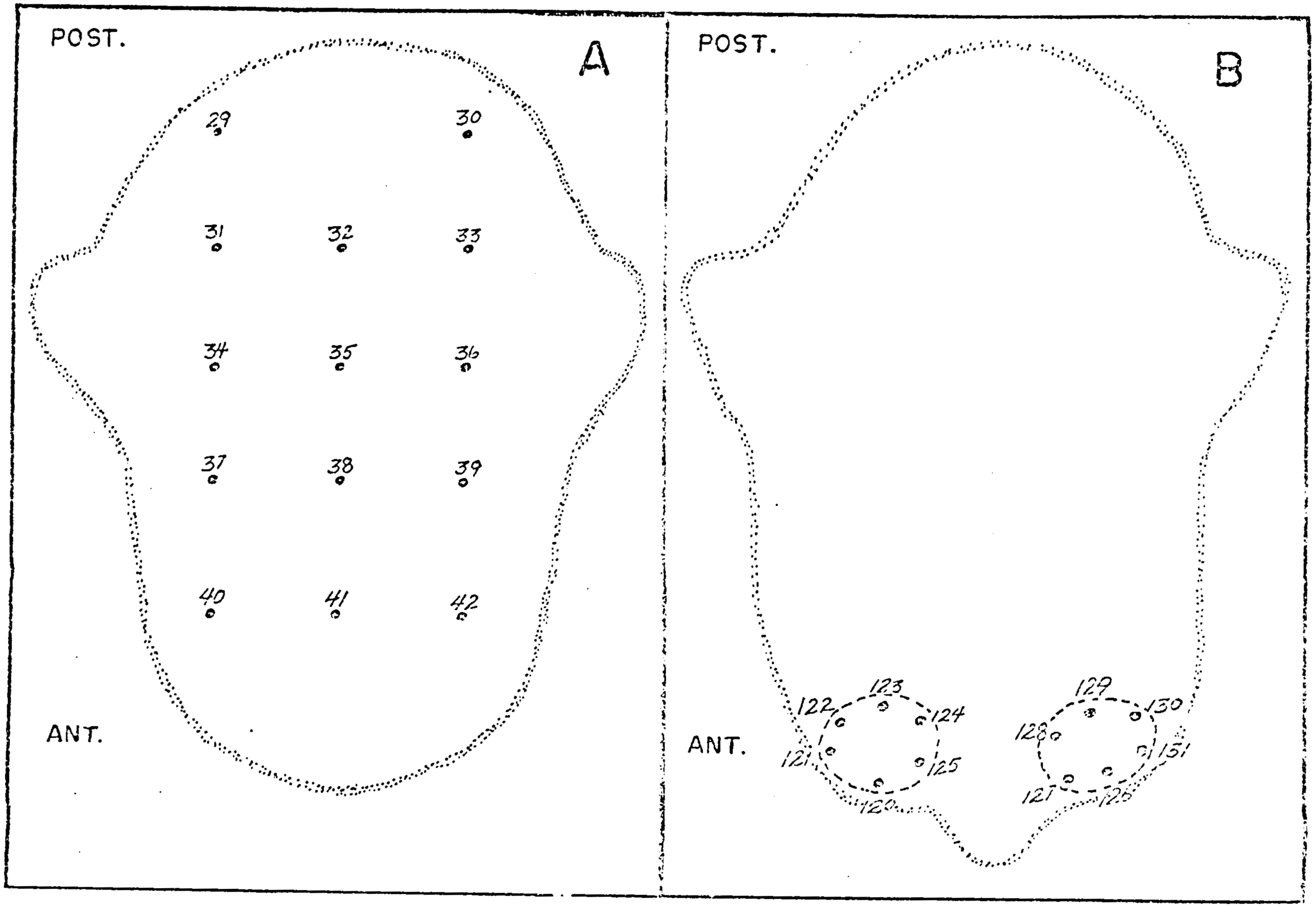


Fig. 19B. Number and location of holes for slab 3 superior surface (A) and inferior surface (B) of the phantom.

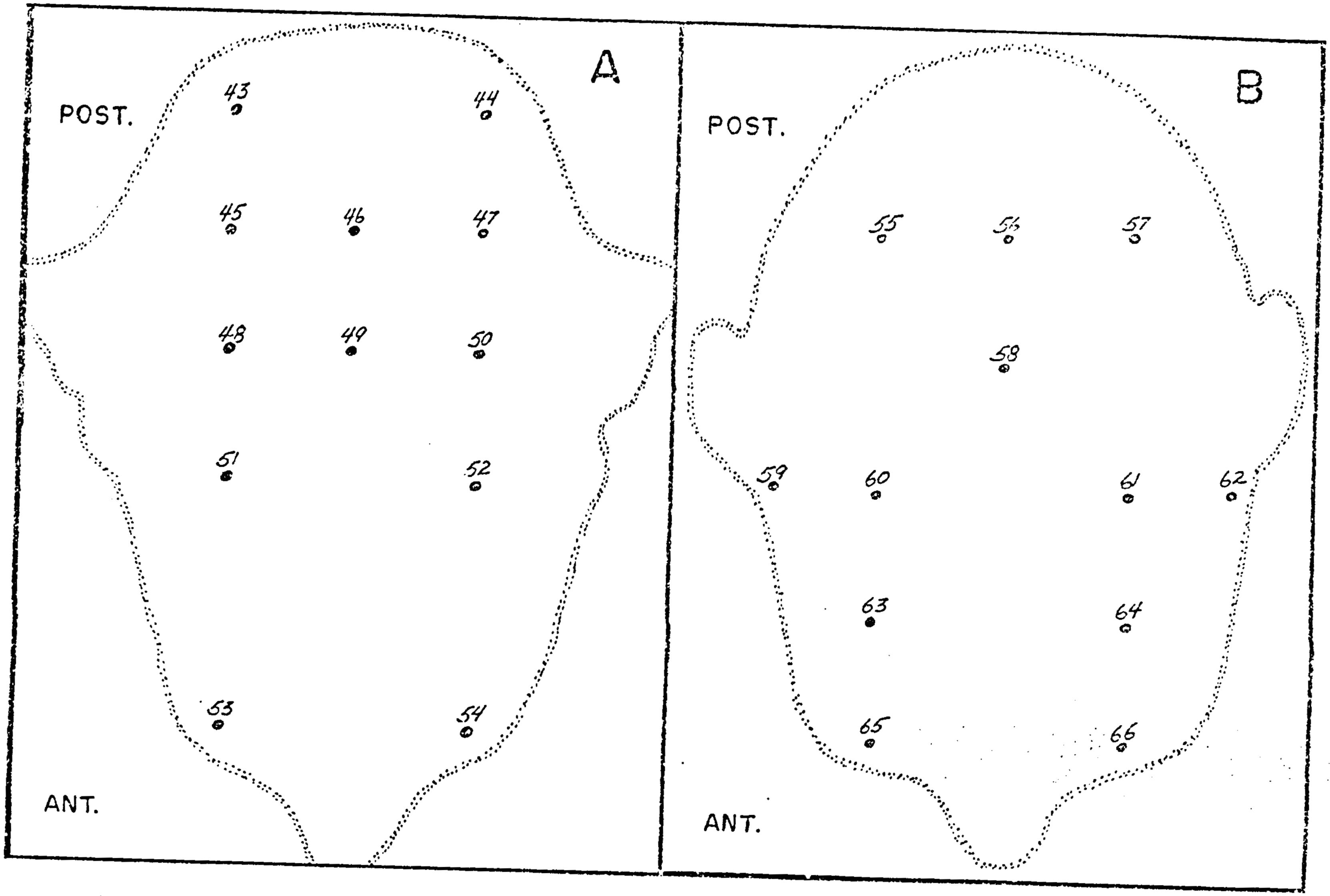


Fig. 20B. Number and location of holes for slabs 4 (A) and 5 (B) superior surfaces of the phantom.

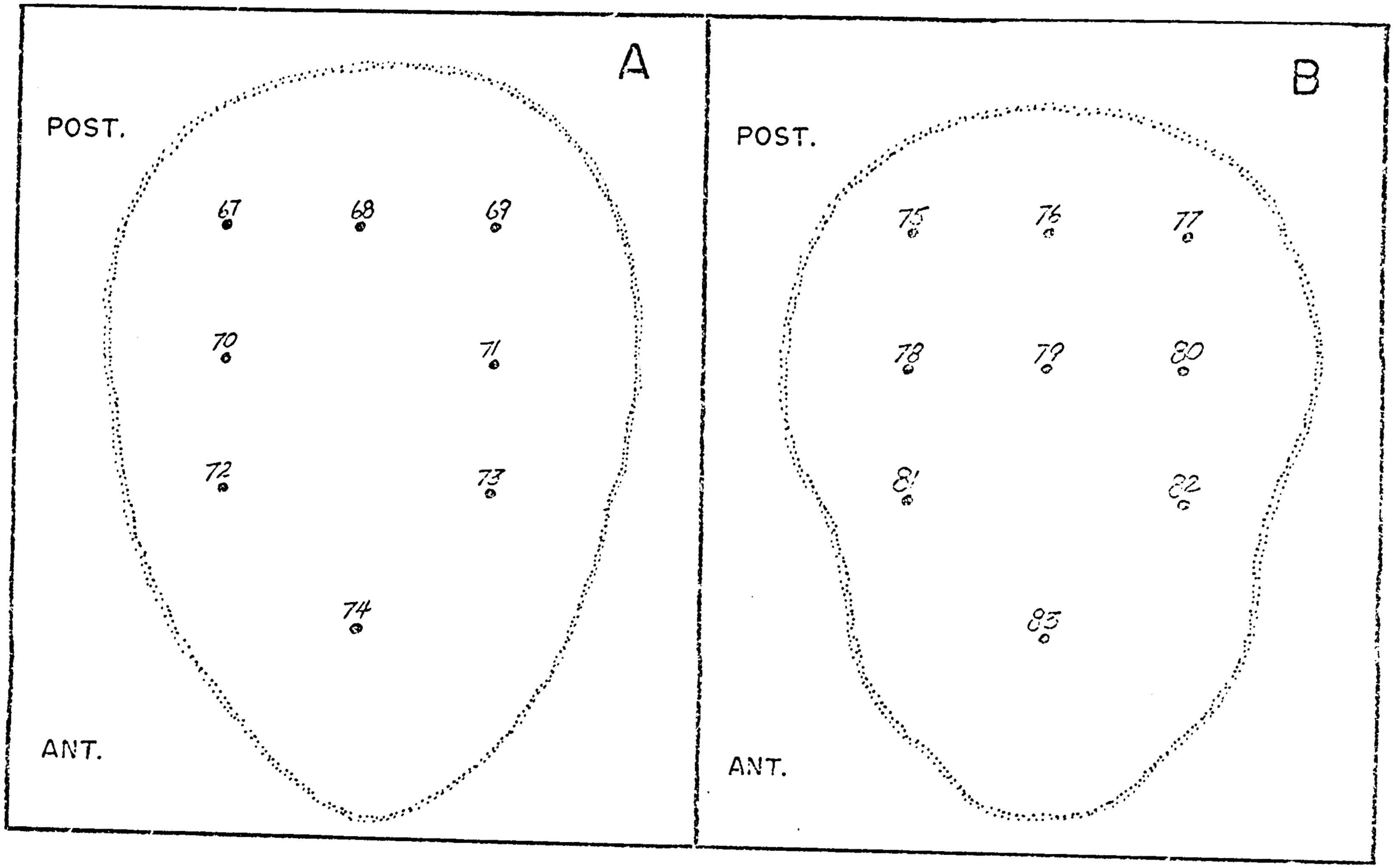


Fig. 21B. Number and location of holes for slabs 6 (A) and 7 (B) superior surfaces of the phantom.

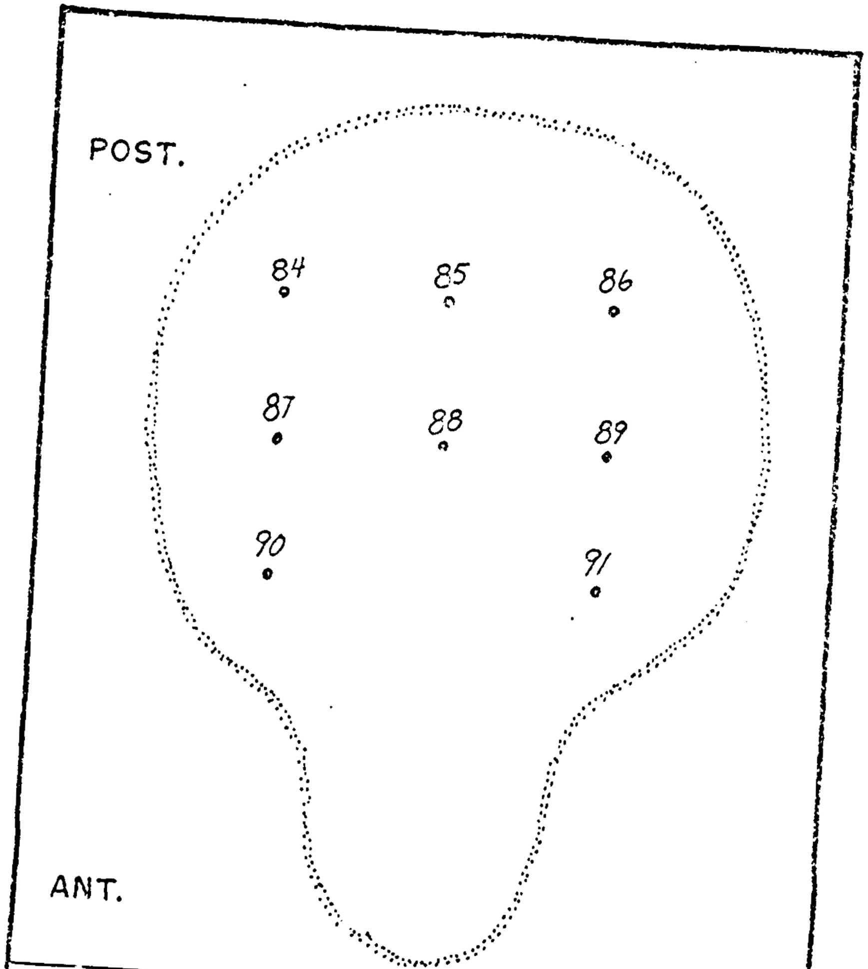


Fig. 12B. Number and location of holes for slab 8 superior surface of the phantom.

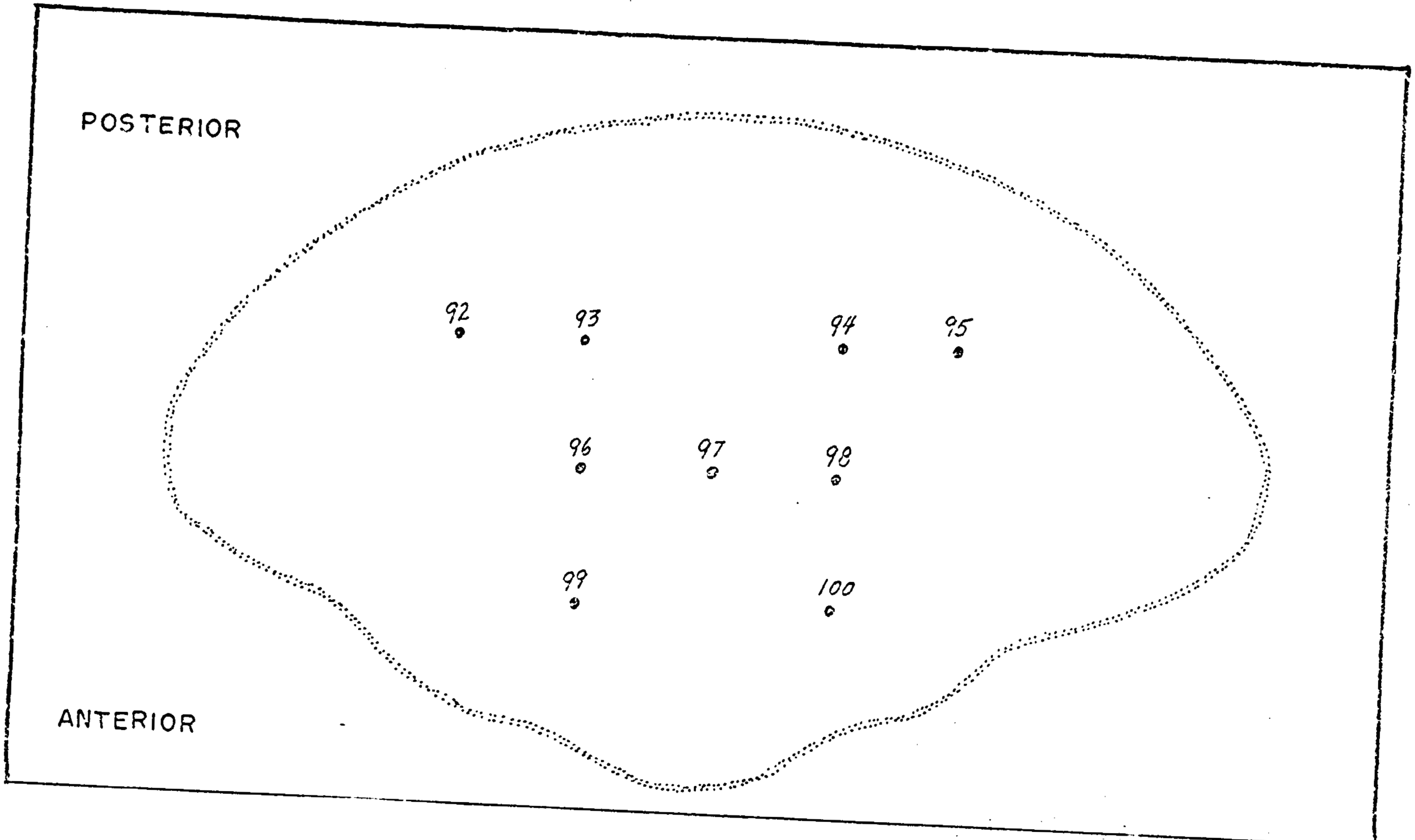


Fig. 23B. Number and location of holes for slab 9 superior surface of the phantom.

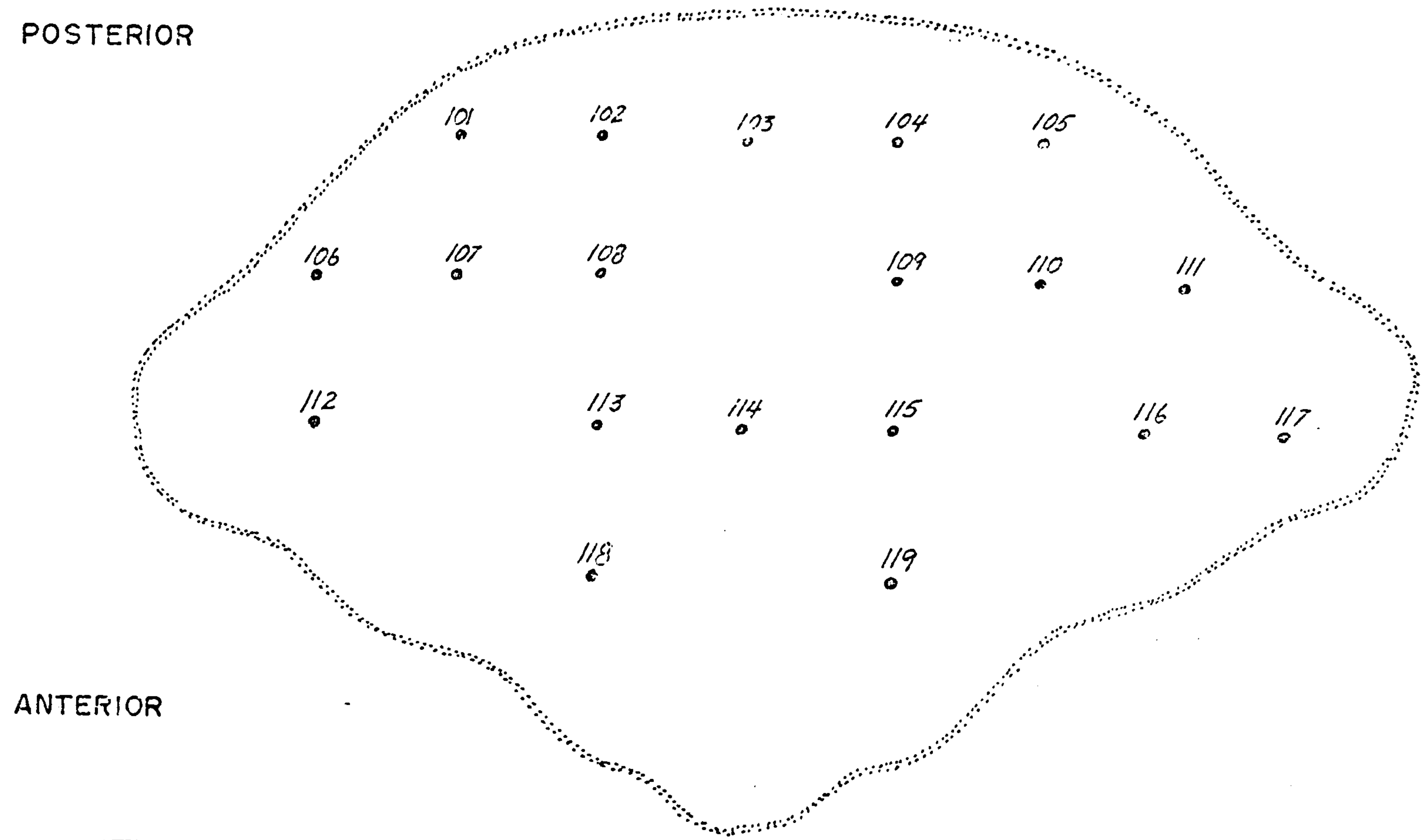


Fig. 24B. Number and location of holes for slab 10 superior surface of the phantom.

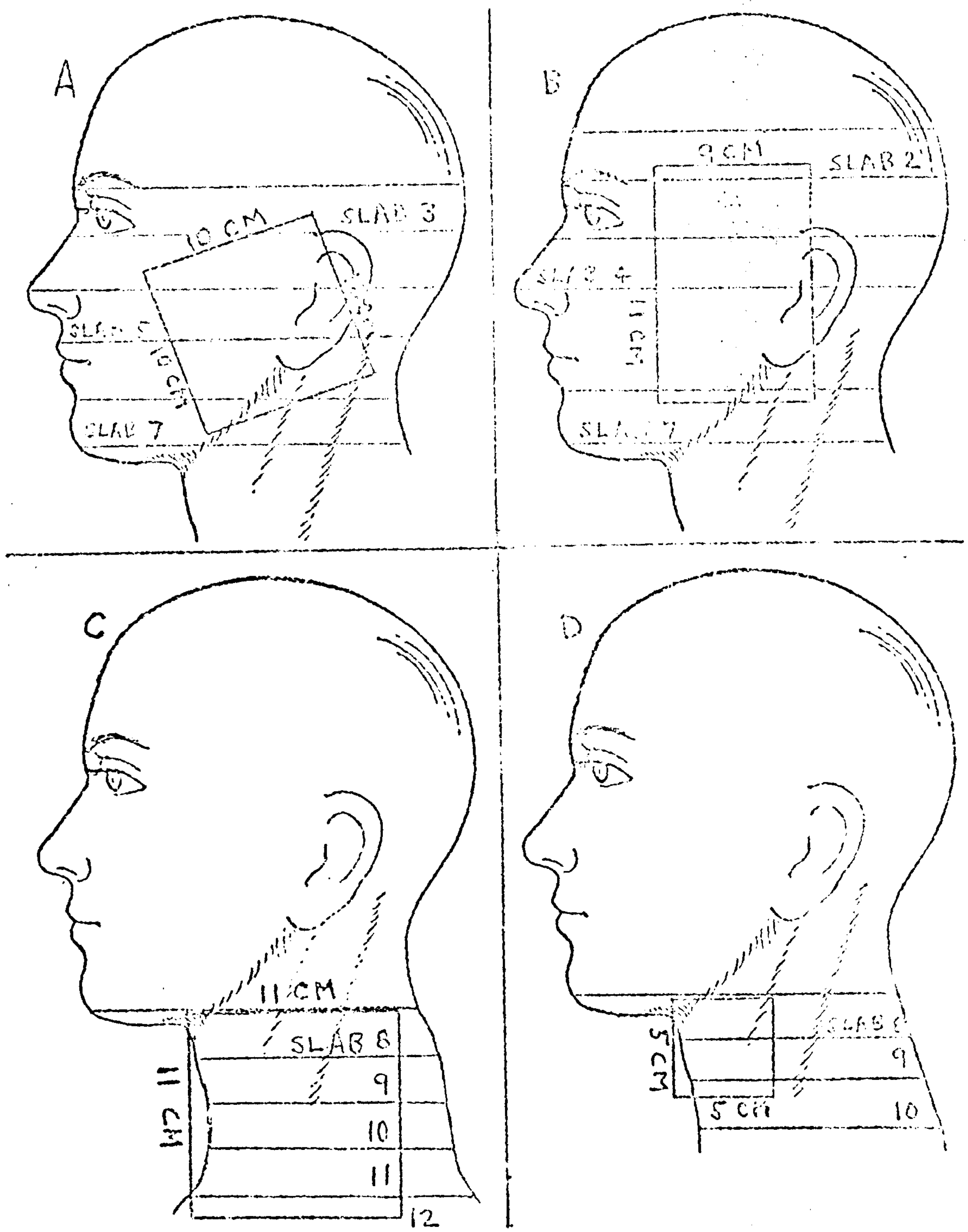


Fig. 25B. Shape, size, and location of treatment fields for four patients: A ($\underline{S}$1), B ($\underline{S}$ 2), C ($\underline{S}$ 3), and D ($\underline{S}$ 5).

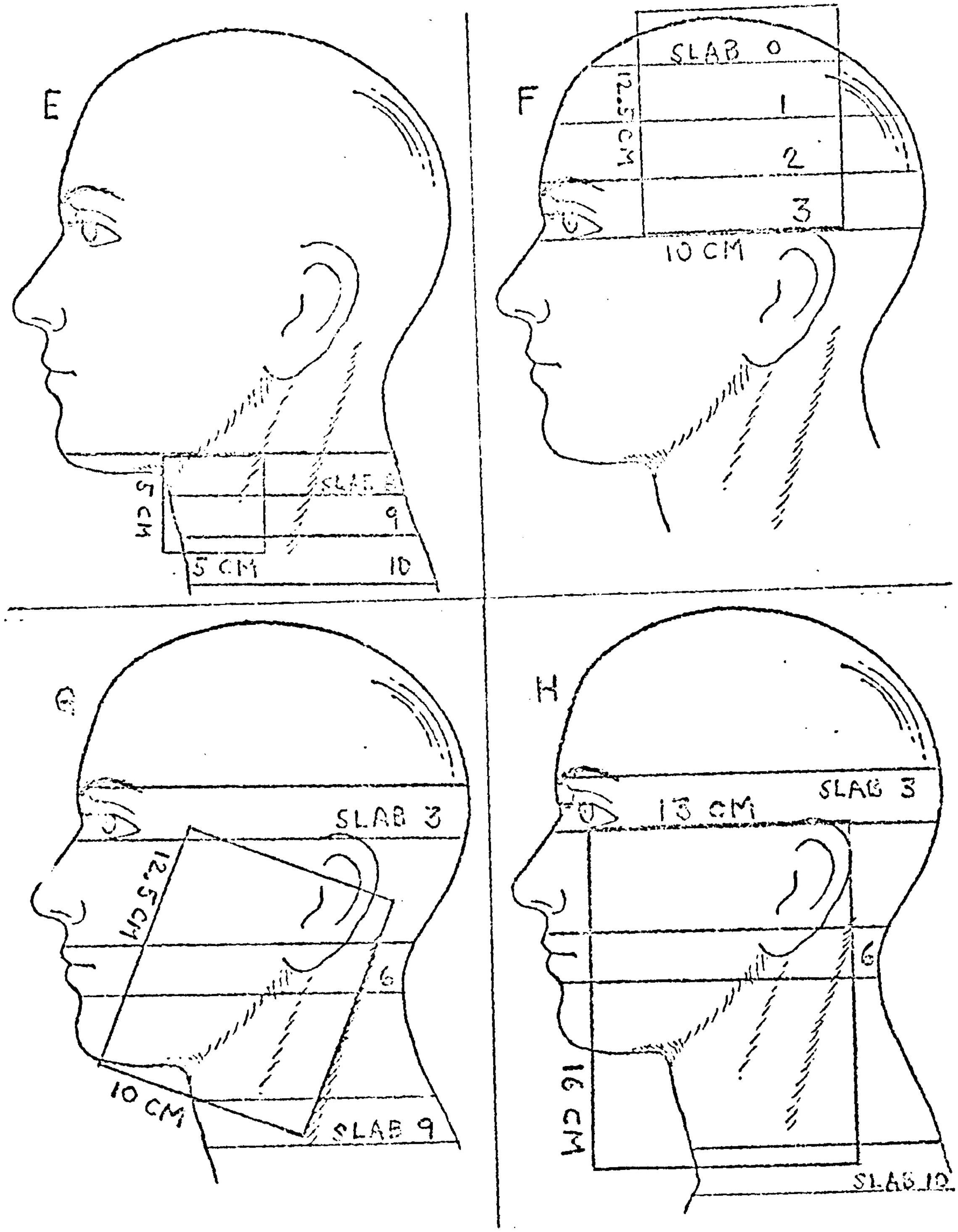


Fig. 26B. Shape, size, and location of treatment fields for four patients: E (S 6), F (S 7), G (S 8), and H S 9).

trichloroethylene prior to the methanol rinse.

The initial treatment field was irradiated 8 times to arrive at an estimate of variation in the measurements. All subsequent fields were irradiated at least twice and mean values were determined for each of the 131 points in the phantom.

Results

The mean measured exposure in Roentgens was converted to dose in rads using an F value of 0.957 for Cobalt-60 and muscle (Smith _et al._, 1964). The doses and dose rates at certain locations of interest have been presented in Table 3 (page 22). Table 1B shows the mean exposure for each of the 131 points for each of the patients and clinical geometries used. The estimated overall accuracy of the measurements is $\pm$ 5%.

Table 1b

The Mean Measured Exposure (R) at Each of the 131 Points in the Rando-Alderson Phantom for Each of the Eight Ss Reported in This Study[1]

Slab No.	Hole No.	Mean Exposure (R) in Each Hole (Subjects) 1	2	3	5	6	7	8	9
1	1	5	6	2	0.7	0.8	46	4	6
	2	5	6	2	0.7	0.8	46	4	6
	3	5	6	2	0.7	0.8	46	4	6
	4	6	12	2	0.7	0.8	258	6	9
	5	7	14	2	0.7	0.8	270	6	10
	6	6	11	2	0.7	0.8	270	6	9
	7	9	31	2	0.7	0.8	295	6	12
	8	9	24	2	0.7	0.8	307	6	13
	9	9	23	2	0.7	0.8	307	7	12
	10	10	27	2	0.7	0.8	307	7	12
	11	10	28	2	0.7	0.8	307	7	12
	12	11	27	2	0.7	0.8	305	7	12
	13	8	21	2	0.7	0.8	289	7	12
	14	7	14	2	0.7	0.8	58	5	11
2	15	7	10	2	0.7	0.9	46	5	9
	16	7	9	2	0.7	0.8	46	5	9
	17	11	30	2	0.7	0.8	243	8	20
	18	12	39	2	0.7	0.8	249	8	24

[1]The values shown resulted from exposing the phantom bilaterally. One field was irradiated, the phantom was then turned 180°, and the opposite field was irradiated. The values shown are thus representative of two daily radiation sessions (treatments); the exposure delivered during any one data gathering period was one-fourth the values reported in the table

Table 1B (continued)

Slab No.	Hole No.	Mean Exposure (R) in Each Hole (Subjects) 1	2	3	5	6	7	8	9
	19	10	33	2	0.7	0.8	267	8	19
	20	38	171	3	0.7	0.8	301	11	45
	21	28	129	3	0.7	0.8	307	10	39
	22	34	148	3	0.7	0.8	295	11	41
	23	57	156	3	1.0	0.8	307	13	41
	24	64	144	3	1.0	1.0	310	13	41
	25	62	150	2	1.0	1.0	313	13	43
	26	31	142	2	1.0	1.0	267	16	39
	27	34	147	2	1.0	1.0	274	16	41
	28	33	131	2	1.0	1.0	282	15	36
3	29	8	13	3	1.0	1.0	40	7	15
	30	7	12	3	1	1	46	6	15
	31	24	59	3	1	1	230	15	77
	32	22	59	3	1	1	230	17	87
	33	22	63	3	1	1	230	17	86
	34	108	238	3	1	2	249	31	183
	35	101	255	3	1	2	258	33	186
	36	105	247	3	1	2	246	35	186
	37	224	274	3	1	2	289	50	175
	38	253	283	3	1	2	282	50	203
	39	260	323	3	1	2	276	49	183
	40	165	308	3	1	2	246	50	226
	41	139	281	3	1	2	246	68	190
	42	141	285	3	1	2	246	67	190
4	43	10	14	3	1	2	25	10	22
	44	10	13	3	1	2	25	9	20
	45	41	66	6	1	2	92	47	117
	46	46	64	6	1	2	126	49	130

(Table continued on following page)

Mean Exposure (R) in Each Hole

Slab No.	Hole No.	1	2	3	5	6	7	8	9
	47	43	64	6	1	2	114	49	123
	48	233	272	6	1	2	117	168	280
	49	221	292	6	1	2	135	166	292
	50	224	282	6	1	2	135	152	294
	51	330	310	6	1	2	150	259	330
	52	330	310	6	1	2	110	259	325
	53	221	75	6	1	2	28	90	355
	54	233	73	6	1	2	27	92	334
5	55	84	72	6	1	2	26	100	164
	56	75	69	6	1	2	28	101	161
	57	68	66	6	1	2	28	94	155
	58	305	281	6	1	2	34	316	339
	59	333	330	6	1	3	28	365	323
	60	330	329	6	3	3	28	348	328
	61	330	300	6	3	3	25	363	354
	62	331	300	6	3	3	25	355	351
	63	348	318	6	2	3	28	406	359
	64	346	304	6	2	3	25	365	350
	65	195	76	6	2	2	12	164	364
	66	247	73	6	2	2	12	165	358
6	67	115	73	14	2	2	9	67	173
	68	117	66	11	2	2	9	71	180
	69	118	65	14	2	2	9	67	163
	70	319	280	14	3	3	9	321	361
	71	303	279	14	3	3	9	333	315
	72	362	293	14	5	6	9	370	374
	73	348	300	11	5	6	9	373	360

(Subjects) spans columns 1–9.

(Table continued on following page)

Slab No.	Hole No.	Mean Exposure (R) in Each Hole (Subjects) 1	2	3	5	6	7	8	9
	74	332	290	11	5	6	9	365	348
7	75	50	44	17	3	4	6	71	244
	76	60	55	15	3	4	6	70	234
	77	49	39	45	3	4	2	59	221
	78	168	124	56	11	15	2	333	343
	79	145	122	64	11	15	2	325	345
	80	165	136	50	9	13	2	348	347
	81	302	127	56	46	55	2	420	373
	82	311	140	56	41	52	2	420	373
	83	220	121	61	48	58	2	424	388
8	84	12	11	164	4	6	3	36	173
	85	16	11	167	4	6	3	40	192
	86	12	10	167	4	6	3	34	190
	87	29	19	245	35	47	6	253	328
	88	33	23	231	30	42	6	300	328
	89	32	23	239	32	44	6	282	337
	90	52	21	261	293	350	6	405	373
	91	59	25	253	270	330	6	430	415
9	92	7	5	161	4	6	3	21	153
	93	7	6	167	4	6	3	21	147
	94	7	5	170	4	6	3	21	172
	95	7	5	136	4	6	3	21	138
	96	9	8	242	41	50	3	165	287
	97	9	8	236	41	50	3	164	282
	98	9	8	242	41	50	3	165	307
	99	20	8	286	372	384	3	337	344
	100	14	8	270	353	384	3	337	334
10	101	4	3	25	2	3	2	8	18
	102	4	2	28	2	3	2	8	18

(Table continued on following page)

Slab No.	Hole No.	Mean Exposure (R) in Each Hole (Subjects) 1	2	3	5	6	7	8	9
	103	4	2	28	2	3	2	8	16
	104	3	3	28	2	3	2	8	17
	105	4	3	28	2	3	2	8	16
	106	4	4	133	3	4	2	11	68
	107	4	4	114	3	4	2	11	58
	108	4	3	122	3	4	2	11	71
	109	4	4	126	3	4	2	11	84
	110	5	4	139	3	4	2	11	91
	111	5	4	126	3	4	2	11	71
	112	6	5	228	12	19	2	33	97
	113	6	6	206	14	22	2	37	113
	114	5	5	145	12	18	2	30	107
	115	5	4	153	12	19	2	33	123
	116	5	5	157	14	19	2	35	149
	117	6	5	206	11	19	2	35	95
	118	5	5	236	98	130	2	55	151
	119	6	5	253	87	127	2	55	171
3	120	130	56	3	1	2	31	53	270
left	121	160	148	3	1	2	55	105	280
eye	122	227	231	3	1	2	98	155	287
	123	214	242	3	1	2	111	177	270
	124	183	178	3	1	2	77	145	204
	125	157	95	3	1	2	46	81	291
3	126	92	48	3	1	2	28	50	283
right	127	145	84	3	1	2	43	71	291
eye	128	176	185	3	1	2	71	132	280
	129	202	210	3	1	2	92	149	316
	130	188	204	3	1	2	83	145	295
	131	143	99	3	1	2	46	81	309

END

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